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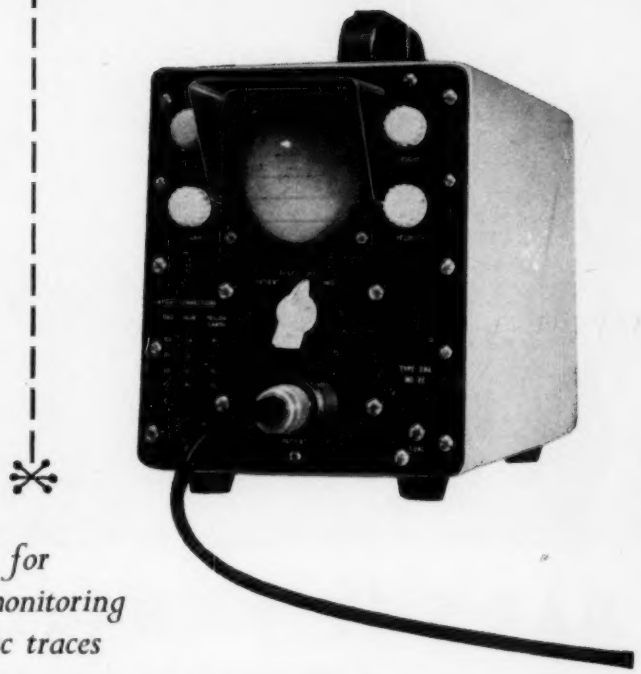

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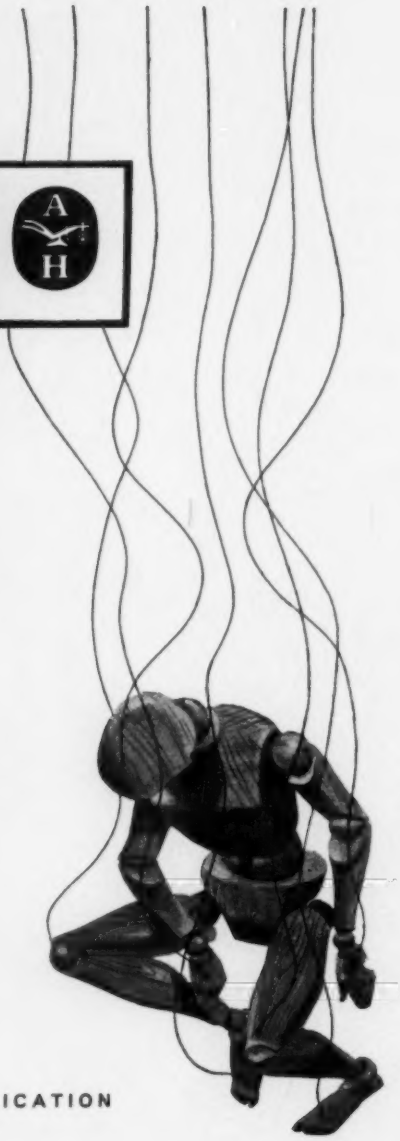

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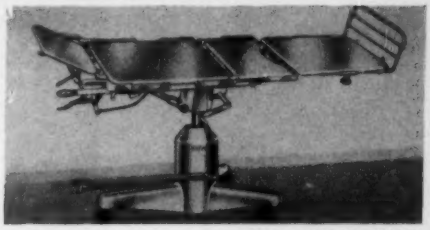

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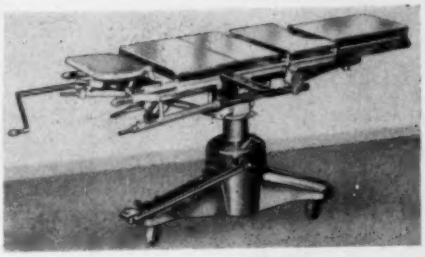

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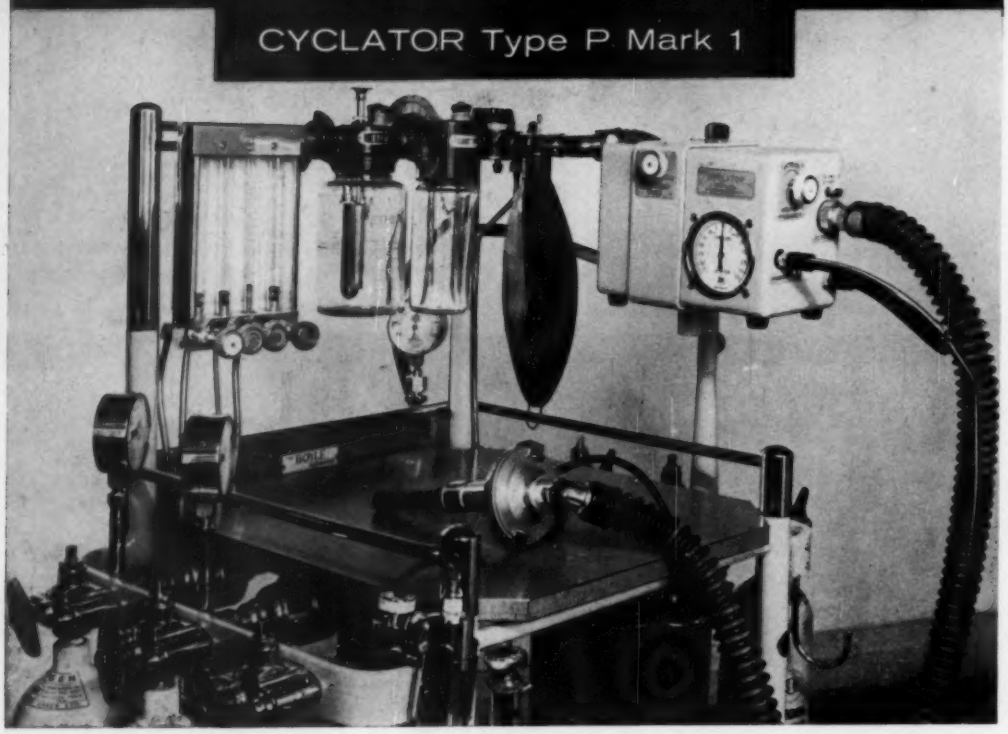

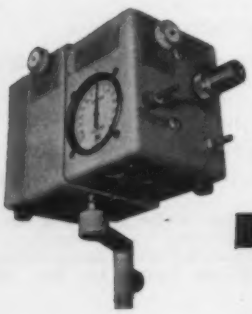

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXIII, No. 10 OCTOBER 1961

EDITORIAL

CIRCULATORY FIRST AID

NOT long ago the anaesthetist received a somewhat gruesome addition to his armamentarium—a knife—and, as a result, some of our more intrepid colleagues have invaded surgical territory with good effect.

Had the technique of cardiac massage come into its own at the time of the celebrated Hyderabad controversy, the Nizam might not have dug so deeply into his pocket, and the lives of thousands of small animals would have been saved from "physiological" experiments at a high altitude!

Advances in resuscitation continue apace and now the anaesthetist can "down tools" so to speak, for a knife is no longer essential and he can, at the expense of a few ribs, perhaps, massage the heart without drawing a drop of blood, *and with his bare hands*.

In these days of incredibly fast advances the doctor tends to have his own senses substituted by impressive instrumentation, and it is therefore all the more refreshing to find that anaesthetists' hands can establish a circulation by squeezing the heart between the sternum and vertebral column. Once this is effected, however, there may be difficulty in stimulating the heart to continue its own beat. External defibrillation is now possible and this means it may not be necessary to open the chest.

Elijah, though quick to direct his prophetic breath into the lungs of the widow's son, might have paused for longer—perhaps with disastrous consequences—had he been aware of what was to take place later in the field of resuscitation. Following in Elijah's footsteps the rescuer now uses his own bellows (or built-in respirator)—as he pauses in compressing the heart some sixty times a minute—to inflate the patient's lungs. So with blows of one kind and another, that which is good in the air may be brought by dint of unusual effort to the place where it is most sorely needed—the cerebrum.

To anaesthetists these things fall naturally into place, but what of the layman who takes a special and active interest in first aid? Should he be taught these measures?

The film "That They May Live" is a good exposition of how a simple technique for artificial respiration may be taught to lay persons, and another film deals with external cardiac massage and shows an equally simple technique. There is no doubt that lay persons are being made aware of these procedures, and a time may come, if indeed it is not already present, when an ordinary faint in the street may cost a man a broken rib or two. This would not matter overmuch, provided no other complications ensued and the heart had really stopped! But to end up with a haemothorax, a ruptured liver or a surgical emphysema is a fine price to pay for a faint.

However, it seems unlikely that a lay person would mistake a man in a swoon for a dead one. But this has happened in hospitals! Cardiac pulsation may be difficult to detect, especially in obese people. To decide the issue is not always easy for those who are constantly on the alert, even when they are provided with a pulsometer or an e.c.g. apparatus.

The decision has to be made by the person on the spot. Action must be quickly taken and it would seem wise to assume cardiac arrest when no pulse can be felt either in the neck or limbs. Nothing attempted nothing done, and in these circumstances first aid is final aid.

Brit. J. Anaesth. (1961), 33, 480

PHYSIOLOGICAL ASPECTS OF CIRCULATORY ARREST AND RESUSCITATION

BY

GERALD R. GRAHAM

Department of Clinical Physiology, Hospital for Sick Children, Great Ormond Street, London, W.C.1

INTRODUCTION

"CARDIOVASCULAR resuscitation", in the context of this discussion, refers to the re-establishment of a normal circulation throughout at least the so-called vital organs following the sudden failure of the heart to sustain an adequate output of blood.

Acute and chronic factors.

The inability of the heart to maintain or make use of its contractile powers may be the result of some sudden event or the consequence of a chronic impairment of normal functions which suddenly, if only momentarily, precipitates complete cessation of activity.

Although diagnostically and therapeutically the differentiation between the "acute" and "chronic" factors which have led to circulatory arrest is important and may even be crucial, any physiological consideration of the problem must remain focused upon the mechanisms responsible for—in the final stage of functional failure—circulatory arrest. This arrest, which prevents adequate blood flow from reaching the tissues, may be due to impairment or failure of the heart as a pump in not being able to propel a sufficient quantity of blood in a given time, or it may be the result of a more or less sudden reduction of the amount of blood which becomes available to the heart as venous return: haemorrhage is the simplest and most direct example of the latter mechanism.

Cardiac and extracardiac factors.

The division into cardiac and extracardiac causes of circulatory arrest is highly artificial. First of all, the propulsive power of the heart and the amount of blood pumped by it is the main determinant of venous return. Secondly, any marked depletion of blood volume—whether through haemorrhage, severe intravascular pooling or loss of plasma, as in burns—weakens the contractile, and thus propulsive, power of the heart by decreasing coronary flow secondarily as a result of an inevitable associated fall in arterial blood pressure. Cardiac and extracardiac factors thus tend to reinforce one another in a vicious circle, no matter which was the primary cause, until circulatory arrest supervenes. In an acute catastrophe this vicious circle may take but a few seconds to be established, for the moment irreversibly, until outside intervention can break it. To this extent then the terms circulatory arrest and cardiac arrest can be considered as synonymous and will be so used, although in a given situation the primacy of a cardiac or extracardiac factor may be given special note.

Oxygen-carrying function of the circulation: interrelationship between circulation and respiration.

The circulation, as the transport system of the body, carries various nutrients—essential and non-essential—to the many tissues and organs of the body, blood being the carrier medium. But it is only with regard to its conveyance of oxygen that even a momentary failure of delivery can be said to bring about an emergency situation. Stated obversely, the fundamental problem of circulatory arrest is the sudden deprivation of vital organs of oxygen essential to their proper function and even survival. The problem of circulatory arrest and thus of resuscitation is therefore inextricably interwoven with the maintenance or re-establishment of respiration. On a practical level, cardiovascular resuscitation includes respiratory resuscitation. For that matter, respiratory failure often actually pre-

cedes and is the cause of circulatory (primarily cardiac) failure.

These two functions, circulation and respiration, are but two aspects of the same task especially when viewed as an acute problem: the provision of oxygen to vital organs. Any attempt to attend to one aspect while ignoring the other is bound to lead to failure. Even minimal blood-flow may oxygenate a tissue adequately, if full use is made of the oxygen-carrying powers of blood and plasma; while, on the contrary, a normal blood supply is practically useless if the amount of oxygen carried is deficient. It is worth while to consider that, from the point of view of an organ or tissue, it is ultimately not the rate of oxygen supply, rate of blood flow or oxygen content which is of crucial importance, but the total amount of oxygen supplied to it: a "trickle" of blood fully oxygenated or "hyperoxygenated" (i.e. also carrying oxygen dissolved in plasma) may supply more oxygen in a given time than a "normal" flow of poorly oxygenated blood. Hence the need and value of a good oxygen supply to the lungs even before a good circulation is known to be present.

The physiological considerations which must govern any discussion of cardiovascular resuscitation include (1) primary and secondary factors causing, or at least favouring, circulatory arrest; (2) direct and immediate effects of arrest on the heart itself and on other tissues and organs; (3) factors favouring or preventing a successful reversal of arrest; and (4) likely sequelae of arrest. These aspects will be presented in the following pages, after a description of those functions of the normal circulation which are involved in any arrest.

EVIDENCE OF A NORMAL CIRCULATION

The two obvious, i.e. immediately accessible, signs of an adequate circulation are a satisfactory colour of the skin and visible mucous membranes, and a normal blood pressure (or easily palpable peripheral pulse) with a regular heart rate.

Systemic blood pressure and heart rate.

These constitute the simplest of all circulatory functions to measure; they are at the same time the most useful and most treacherous indicators. For the blood pressure and heart rate are themselves the resultants of a number of cardiovascular functions, any one of which may be profoundly affected without this being obviously reflected in any changes of blood pressure or heart rate. In particular, the measurement of arterial pressure should never be made without full weight being given to (*a*) heart rate and (*b*) pulse pressure (the difference between systolic and diastolic pressure). For example, the first and immediate compensatory mechanism in response to a rapid diminution in circulating blood volume (as after rapid bleeding), to a sudden profound vasodilation or to failure to constrict, or to sudden myocardial failure (to name one central and two peripheral causes) is an increase in heart rate, mediated reflexly via the carotid sinus and aortic arch receptors which are sensitive to even slight changes in the level and "shape" of the systemic blood pressure.

The resultant rise in heart rate usually manages to return the momentarily lowered pressure towards normal values (although the pulse pressure may be narrowed), if only temporarily. A consideration of both the blood pressure and heart rate immediately provides the clue to the compensation which has been called into play and thus warns of the underlying event. Associated with the heart-rate response in the described situation is peripheral vasoconstriction, signified by a pale and cold skin, the other of the two signs already mentioned, which is thus of itself a clue to the underlying circulatory compensation.

Regional flow.

If a normal blood pressure has been achieved through tachycardia and peripheral vasoconstriction, this does not necessarily imply an even relatively adequate blood supply to some vital organs, although their vascular system may not participate in the vasoconstriction: in fact, the "purpose" of the outlined compensation is generally seen to lie in the provision of an adequate head of pressure for the perfusion of the vital organs (brain, heart, liver and kidneys). But this formulation overlooks the fact that a normal blood pressure (however maintained) tells us little about the *amount* of blood (and thus oxygen) going even to the privileged vital organs. Cardiac output, and thus regional flow, may be woefully low yet the blood pressure within normal range. Herein lies the fallacy of placing too much reliance upon the blood pressure, unless its meaning be critically assessed.

One important secondary aspect, which concerns the coronary circulation, must not be overlooked. The main determinant of coronary arterial inflow is the work of the heart (or its energy expenditure). At identical systolic blood pressure levels the work of the heart, and thus the coronary flow, is increased with rising heart rate, always presuming that the coronary arterial bed is capable of dilating and thus receiving the needed flow increment. This it may, however, not be able to do in coronary arteriosclerosis, which restricts and fixes the lumen of the affected vessels. Hence the dangers of an increased heart rate as a compensating mechanism in those with coronary artery disease: sudden coronary insufficiency may result and lead to dangerous arrhythmias. Cardiac resuscitation in these and similar circumstances may be difficult.

Matters are slightly different with respect to the cerebral circulation. While the mean blood pressure provides the head of pressure—the minimum requirement, as it were—the most profound changes are brought about by alterations in blood tensions of oxygen and, especially, carbon dioxide: breathing a mixture of 5–7 per cent of carbon dioxide in air causes a 75 per cent increase in cerebral blood flow, while breathing a 10 per cent oxygen mixture causes a rise in cerebral blood flow of about 40 per cent. Any circulatory or respiratory arrest or impairment thus immediately causes profound cerebral vasodilatation and places the brain in a favourable position to receive whatever little blood is flowing and able to deliver oxygen.

Heart sounds.

Auscultatory evidence of a normal circulation is only of limited value and must be assessed in conjunction with palpation of the peripheral pulse. The presence of heart sounds is of help largely as a measure of heart rate and rhythm. Neither their quality nor their intensity is a reliable sign for the effectiveness of cardiac activity, although an abrupt change of either, under one's ear as it were, is of significance. The absence of heart sounds, unless one has reason to suspect the presence of conditions interfering simply with their transmission to the chest-wall, is an indication of either cardiac asystole, ventricular fibrillation, paroxysmal ventricular tachycardia with a high and ineffective rate of ventricular contractions, or a very low blood pressure: if this is below about 50 mm Hg heart sounds are often difficult to hear or inaudible, especially in the presence of a noisy respiration.

Cyanosis.

As useful and limited as the determination of blood pressure and heart rate is the evidence of skin colour.

Some of the implications of skin pallor have already been mentioned. The appearance of cyanosis of the skin and mucous membranes will, in the absence of some types of congenital heart disease, indicate either peripheral vascular stasis (profound desaturation of blood in situ) or inadequate oxygenation of arterial blood in the lungs, as a result of airway obstruction, deficient pulmonary ventilation or blockage of oxygen transfer from alveoli to pulmonary capillaries. Since the appearance of cyanosis depends on the presence of a minimum of reduced haemoglobin (very approximately, 5 g) it may be late in onset or absent in states associated with anaemia. Furthermore, there is an appreciable observer's error involved in its recognition. Its absence is thus of little value for judging the state of the circulation. None the less, when present (especially, if it suddenly develops) it is a sign of the greatest importance, because—no matter whether its primary cause is circulatory or respiratory—its continuance is an indication that insufficient oxygen is reaching the organs, i.e. it signifies severe hypoxaemia and thus threatened hypoxia. The sudden development of cyanosis invariably warns of the existence of an emergency situation requiring immediate action to restore a normal circulation and assure a patent airway and a normal pulmonary gas exchange.

On the other hand, the disappearance of cyanosis, for example on artificial ventilation with 100 per cent oxygen, does not necessarily imply an adequate oxygen supply to the body, since the blood may be fully oxygenated (and thus not contain reduced haemoglobin) but the rate of flow not enough to provide an adequate amount of oxygen to the vital organs.

SOME FACTORS FAVOURING CIRCULATORY ARREST

As has already been mentioned, cessation of circulation may occur acutely without warning in the absence of known cardiovascular or other disease, or it may be precipitated in the presence of dis-

ease. In either case the immediate results and consequences are the same, although the prognosis is not. It is possible, but rare, for a single cause to be responsible for circulatory arrest: usually an interplay of several factors is involved. Only in extreme conditions will a single event or disorder result in arrest. Thus, profound hypoxaemia, if of more than a few minutes' duration, may cause the cessation of cardiac contraction. In the absence of underlying heart disease it is, however, rare for hypoxaemia to persist long and severely enough to lead to acute heart failure. Hypoxaemia of primary respiratory causation will generally not impair cardiac activity in advance of irreversible changes to the central nervous system. The heart is, in fact, remarkably resistant to acute hypoxaemia *per se*, certainly more so than the cerebral cortex. It will continue to contract relatively effectively after other vital signs have disappeared. Herein lies the opportunity and challenge of cardiac resuscitation; at the same time it reinforces the need to protect those organs more vulnerable to hypoxia.

It is usually the combination of hypoxaemia with direct or indirect impairment of cardiac contractile power which results in cardiac arrest. Obversely, the primary impairment of cardiac contractile power does not usually lead to irreversible arrest, of whatever type, unless primary or secondary hypoxaemia is added to it, as will be explained:

(1) *Vagal stimulation.*

This is known to cause, directly or reflexly, profound bradycardia and even asystole. Yet before vasovagal reflexes are blamed as a cause of cardiac arrest, it should be remembered that experimental evidence has shown that vagal stimulation alone is incapable of sustaining cardiac asystole: the ventricles "escape" its effects on atrial and nodal impulse formation. Hypercapnia, especially if suddenly induced, was found to accentuate the effect of vagal stimulation, and even prevent "vagal escape" (Young et al., 1951). This may be due to a reduction in cholinesterase activity at the acid pH which results from the hypercapnia. The action of hypoxia added upon vagal stimulation remains controversial. Some workers have found it to decrease its effectiveness, presumably by raising the excitability of any ectopic ventricular pacemaker, while others have found the opposite. It is likely that the state of the myocardium at the time of vagal activity is the determining factor in the response: if ventricular myocardial excitability is depressed by disease or the action of drugs, vagal stimulation may fail to be followed by "escape", even in the presence of anoxia. On the other hand, some forms of myocardial disease are themselves responsible for lowering the arrhythmia threshold of the myocardium to anoxia: in such a case a vagal reflex may precipitate a dangerous arrhythmia, because vagal slowing in itself may lead to myocardial anoxia even where none had existed before. But the fact remains that vagal stimulation *per se*, in the normal heart, does not cause lasting asystole. A special case of the potentially life-threatening result of vagal activity is represented by the carotid sinus syndrome, to which some, usually elderly, people are known to be subject. In them the carotid sinus is extraordinarily sensitive to even the slightest distortion or touch and reflexly may cause complete cardiac standstill (i.e. total sino-atrial block) or ventricular standstill from complete atrioventricular block. Such persons quickly lose consciousness, until vagal escape supervenes, as normally it invariably does. But since those subject to this distressing and dangerous condition are generally elderly and thus likely to have other diseases which accentuate the deleterious effects of only temporary circulatory arrest, the syndrome clearly constitutes a possible cause of cardiac arrest requiring resuscitative measures.

(2) *Massive sympathetic discharge.*

This, including the sudden release of large amounts of adrenaline and noradrenaline is not by itself likely to lead to circulatory arrest, either through cardiac asystole, ventricular fibrillation or ventricular tachycardia. However, the presence of existing heart disease would favour such a possibility. The marked rise in blood pressure and heart rate, in themselves physiological responses, by increasing the work load of the heart, may cause an acute coronary insufficiency and thus ventricular arrhythmia if the coronary circulation or myocardium, or both, are restricted in their ability to meet the increased demands (i.e., in aortic stenosis, or coronary artery disease with or without recent myocardial infarction).

Furthermore certain drugs and anaesthetic agents (notably cyclopropane) are known to raise

the sensitivity of the myocardium (i.e. lower the arrhythmia threshold) to adrenaline and noradrenaline.

(3) *Hypoxia and hypercapnia.*

Anoxia is widely blamed more than any other condition as an important, if not *the* cause of cardiac arrest, especially during surgery under anaesthesia. This concept has, however, not gone unchallenged (Reid, Stephenson and Hinton, 1952), and it is true that critical examination of all circumstances does not always sustain the accusation of hypoxia as the central cause. None the less, there is little doubt that hypoxaemia and the resultant tissue hypoxia have often preceded circulatory arrest. How they do this is another matter. Several possibilities exist. First, the immediate response of the cardiovascular system to hypoxaemia (described later) may in the presence of existing heart disease lead to ventricular arrhythmias—and hence ventricular fibrillation—by placing an added work-load on the heart, which in its diseased state it is unable to meet, or by the release of catecholamines which sensitize the myocardium and lower its arrhythmia—and especially its fibrillation—threshold. Secondly, the myocardium itself is sensitive to hypoxaemia and, especially in the diseased state, has only a limited tolerance to it. This does not mean that its contractile powers are easily or quickly impaired, for the contrary is the case, for the heart is well able to sustain a co-ordinated and effective beat in the presence of severe hypoxaemia long after other tissues (notably of the central nervous system) have been irreparably damaged. The diseased myocardium, however, is highly sensitive not only to hypoxaemia *per se*, but in particular to differences in oxygenation between its various layers. Such local or generalized areas of hypoxia lower the arrhythmia threshold of the ventricular myocardium and may thus precipitate ectopic beats, paroxysmal tachycardia and, eventually, fibrillation—if the underlying hypoxaemia goes unchecked or even becomes more pronounced.

Hypercapnia alone is surprisingly free of effects on the myocardium likely to cause circulatory arrest. However, it may sensitize it to the effects of the catecholamines and may lower the fibrillation threshold in the presence of certain drugs. Furthermore, hypercapnia leads to a fall in blood pH and an associated rise in potassium concentration of the blood, and thus indirectly causes arrhythmias. However, it is not so much the presence of a high carbon dioxide concentration which is to be feared and thus avoided, but a sudden lowering of it. This almost invariably leads to various forms of atrial or ventricular arrhythmia and paroxysmal ventricular tachycardia or fibrillation may result. The post-hypercapnic arrhythmias can be prevented by avoiding any sudden carbon dioxide "blow-off", and can be counteracted by the intravenous administration of sodium bicarbonate solutions. The heart and circulation are otherwise remarkably tolerant to a slow rise in carbon dioxide tension of the blood (Graham, Hill and Nunn, 1960).

(4) *Acute hypovolaemia.*

Any rather sudden reduction in the circulating blood volume—be it from massive haemorrhage, the loss of plasma after extensive burns, or the profound extravasation that follows extensive crush injuries—may lead to circulatory failure and cardiac arrest. The sequence of events leading to this end has obvious therapeutic implications and will thus be described in outline. The immediate result of suddenly developing hypovolaemia (e.g. haemorrhage) is a more or less abrupt reduction in venous return, which can be compensated for in only a limited way by mobilization of blood reservoirs, rerouting of the cardiac output to vital organs, and the diminution of the capacity of the vascular bed by vasoconstriction, especially of the veins.

The inevitable fall in blood pressure, once the compensating mechanisms prove insufficient—which they will, if the haemorrhage is severe—will lead to a fall of coronary circulation *pari passu* with the falling blood pressure and cardiac output. A healthy coronary bed adapts itself well to this situation, responding to a fall in the head of pressure by vasodilatation, in parallel with the energy requirements of ventricular myocardium. The diseased coronary circulation is limited in its adaptability and relative coronary insufficiency may result. This, apart from the dangers of arrhythmia already mentioned, may lead to a weakening of the contractile powers of the heart, and cardiac output will fall further and tissue hypoxia is the inevitable result: a vicious circle is thus established. The margin of safety of even those tissues of the body most sensitive to hypoxia

is such that periods of profound hypotension (mean blood pressure of 40–50 mm Hg) of even 1 hour or more may be tolerated, assuming the absence of complicating factors. But often these additional factors are not known or cannot be evaluated, and the tolerance of the body's tissues to hypoxia cannot be predicted in the individual patient. No reliance must, therefore, be placed on any seemingly "safe" period of hypotension.

The point where irreversibility of circulatory "shock" (to give the period of profound hypotension another name) is reached cannot be fixed in minutes except under experimental conditions. It would seem, however (Freeman, 1961), that where the restitution of a normal or near-normal blood volume is delayed, the hypoxia resulting from the decreased blood supply to the tissues can be mitigated, and the moment of irreversibility delayed, by the provision of as much oxygen as the blood will carry in combination with haemoglobin and dissolved in plasma. The total amount of oxygen supplied is thus raised without any increase in blood flow.

(5) *Electrolyte imbalance.*

There is hardly an electrolyte which, in abnormal amounts under experimental conditions, has not been shown to have profound effects on myocardial performance. And many are the instances where the injection of one or the other solution of electrolytes (various concentrations of calcium, magnesium or potassium salts) has not brought about the restoration of a normal heart beat where other measures (and other electrolyte solutions) had failed previously. It is, however, a long step from these observations to the implication of electrolyte abnormalities as a cause of cardiac arrest. Only the potassium ion can be said to play such a direct role: both in very high and in very low concentrations it is capable of affecting profoundly cardiac conductivity, rhythmicity and contractility with the potential occurrence of cardiac asystole or ventricular fibrillation. Strangely, either high or low potassium concentrations can cause cardiac arrest: the low concentration will generally do so by suppressing pacemaker initiation (i.e., by producing asystole), while the high concentration tends to result in tachycardia and ventricular fibrillation. Paradoxically, however, potassium injected directly into the coronary circulation may cause asystole or the cessation of ventricular fibrillation.

(6) *Other factors.*

Of practical importance in relation to circulatory arrest are profound temperature deviations from normal. Very high fever not only causes marked tachycardia and thus the possible emergence of coronary insufficiency and dangerous arrhythmias in a diseased heart, as already described, but by markedly raising energy requirements may induce relative hypoxia. An abnormally low temperature (hypothermia), on the other hand, increases the chances of arrhythmias and ventricular fibrillation by lowering the arrhythmia threshold. However, this problem is of practical importance only where hypothermia is deliberately applied, a field which can only be mentioned here.

Mechanical stimulation or irritation should be listed as a final factor which may lead to circulatory arrest by causing arrhythmias. In practice, it is only during thoracic operations that this possibility arises. The handling or probing of the myocardium (externally as well as internally) may induce extrasystoles and paroxysmal tachycardia. The surprising fact is, however, that the normal heart is remarkably resistant to the production of any lasting arrhythmia by mechanical stimulation alone. It is only in cardiac surgery, where many complicating factors are added, that cardiac arrest through ventricular fibrillation precipitated by mechanical irritation is an occasional occurrence.

THE EFFECTS OF CARDIAC ARREST ON THE TISSUES

(1) *Hypoxia.*

Two aspects of the problem of hypoxia in relation to circulatory arrest must be clearly separated: hypoxia as a cause of it and the effect of hypoxia once circulatory arrest has occurred. The former has been discussed in the preceding section. The immediate response of the cardiovascular system to hypoxaemia is mediated in the first instance via the medullary centres and leads to an increase in cardiac output from a rise in heart rate and stroke volume. In addition there occurs peripheral vasoconstriction and a rise in systemic blood pressure. These changes compensate for the decreased blood-oxygen content by increasing the flow of blood to the vital organs (i.e., increase the total amount of oxygen delivered), and thus avoid tissue

hypoxia. This, in conjunction with the shape of the oxygen-dissociation curve—which favours the release of oxygen to the tissues even though the oxygen saturation of the blood be lowered—ensures that the oxygen supply to the tissues remains relatively undisturbed for a time. Added to this is the associated response of the respiratory system to hypoxaemia to compensate for the decreased supply of oxygen: the respiratory minute volume (both tidal volume and respiratory rate) is increased, which may aid not only pulmonary gas exchange, but also—via the increased negativity of intrathoracic pressure from the increased ventilatory excursions—venous return to the right heart, and thus it raises cardiac output further (the "respiratory pump").

If circulatory arrest is the cause of the hypoxaemia or if the supply of oxygen to the lungs remains grossly inadequate and cannot thus be compensated for, the result is damage to certain vital tissues, of which the central nervous system, and within it the cortical cells, are the most sensitive. After cardiac stand-still there is a "free interval" of a few seconds during which all tissues still function normally. Unconsciousness supervenes in 8–10 seconds and is then followed, at varying intervals, by seizures and respiratory arrest. The time interval from the moment of damage (withdrawal of oxygen by circulatory arrest or marked hypoxaemia) to cessation of function ("survival time") varies with different tissues, and is dependent on both the level of oxygen requirement for a given tissue and its store of oxygen, or its ability to meet its energy requirements quickly by anaerobic means. The cessation of function in itself reduces the energy requirement to a much lower level, but usually not to zero. The length of time, from cessation of function to restoration of its energy (oxygen) supply still compatible with ultimate complete recovery ("revival time") depends upon the condition preceding arrest (previous damage) and the nature of the tissue involved (fig. 1). There is a general relationship between the time until cessation of function and the duration of such functional suspension which can still lead to complete functional revival: the longer the one, the more protracted the other.

In the case of the heart, an additional complicating factor presents itself in that this organ constitutes at one and the same time the motive force and one of the recipients of the circulatory supply of needed oxygen—once it has again become available—either through cardiac resuscitation or the removal of any obstruction to a normal respiratory exchange. But the heart, though it may resume its beat after a period compatible with complete recovery after ideal circumstances, may not be able at once to provide the contractile power which it possessed before circulatory arrest: after total coronary ischaemia of 3–4 minutes cardiac action is usually too weak to bring about a normal circulation unaided, and seemingly successful cardiac resuscitation may be followed by a "relapse".

Thus, although the heart is able to withstand total ischaemia for longer periods than the brain (for parts of which total ischaemia exceeding 4–5 minutes precludes complete recovery), it needs a long recovery time to overcome the phase of insufficiency which invariably follows complete absence of a supply of oxygen. It should be added that the heart, even in asystole, still has a residual energy expenditure which must be met by an outside supply of oxygen, if damage is to be avoided. The energy requirements during ventricular fibrillation are considerably higher than the minimal metabolic level during asystole and constitute a significant level of the normal metabolic needs.

The time needed for full recovery once a normal supply of oxygen is again provided to the tissues is an important consideration in estimating the chances of full recovery, and any measure which "spares" the tissues during this period will aid in this endeavour. Some of these aspects are presented schematically in figure 1.

The existence of a minimal energy requirement after apparently complete cessation of function following circulatory arrest has an important therapeutic implication. The additional damage from anoxia can be minimized if the residual energy requirements of the tissues (and this applies first and foremost to cardiac and cerebral tissue) can be met by a "residual" circulation: even a "trickle" of blood, albeit carrying normally inadequate amounts of oxygen, will suffice to meet this need and, by avoiding this additional insult, may significantly extend the time of anoxia followed by complete recovery. Experimental evidence indicates that in the presence of complete circulatory arrest the application of intermittent positive-negative artificial ventilation alone does

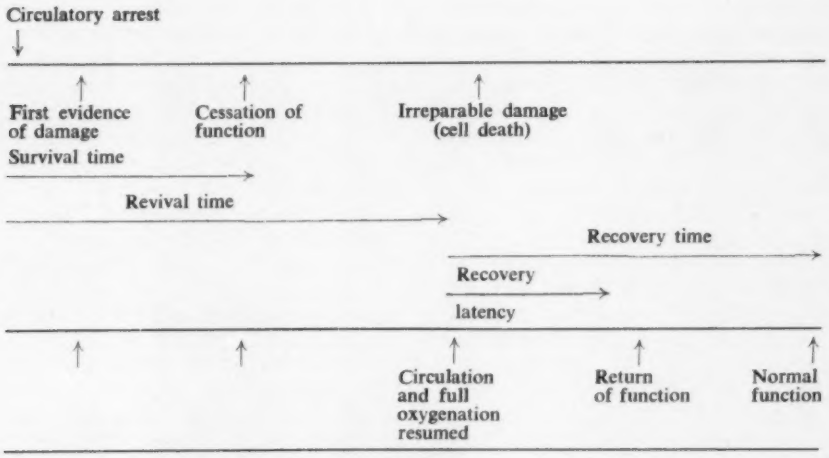

FIG. 1

Schema of the effects of circulatory arrest (anoxia) on the body's tissues. Upper part of diagram shows the sequence to cell death, if oxygen supply is not forthcoming in time; the lower part indicates the steps to normal restitution on resumption of full oxygenation while cells are still capable of revival.

not provide such needed "residual" circulation (Thompson, Quimby and Smith, 1946).

(2) *Hypercapnia.*

The possible effect of this state in favouring circulatory arrest has already been discussed; similar considerations guide the evaluation of the effects of increased blood Pco_2 in this condition. For one thing, the rise in Pco_2 in the blood is only very slow in the presence of the minimal metabolism that exists after circulatory arrest: even at a normal resting level of metabolic activity the alveolar carbon dioxide concentration rises by only about 1 per cent/min. To what extent a rise in blood Pco_2 which has preceded the occurrence of complete circulatory arrest may aggravate the deleterious effects of anoxia is uncertain.

METHODS AND MONITORS OF CIRCULATORY RESUSCITATION

The task of circulatory resuscitation has two aspects: the more direct one of providing artificially, as by cardiac massage, the contractile power of the heart required to supply blood to the body and, secondly, to ensure that this occurs in the presence of an optimal oxygen supply to the blood.

(1) *Methods.*

The type of circulatory arrest (asystole or ventricular fibrillation) requires ultimately different handling, but the emergency measures remain the same. Once it is clear that simple external measures have failed to restore a normal blood supply—in the case of cardiac asystole, a sharp blow on the chest sometimes restores the beat by providing a mechanical stimulus to the heart—cardiac massage must be begun without delay, as even brief anoxic periods at the onset may prejudice later complete recovery. The recent demonstration by Kouwenhoven, Jude and Knickerbocker (1960) that external cardiac massage by rapid compression of the sternum against the spine, thus "squeezing" the heart, can provide an adequate blood pressure and cardiac output has radically changed the chances of successful resuscitation. The simplicity of the method allows anyone to practise it, and the hesitation of the unpractised to open the chest for direct manual cardiac massage and the inevitable delay this usually implies is thus avoided.

This procedure basically differs from that described and successfully applied by Rainer and Bullough (1957). As has been pointed out, a blow

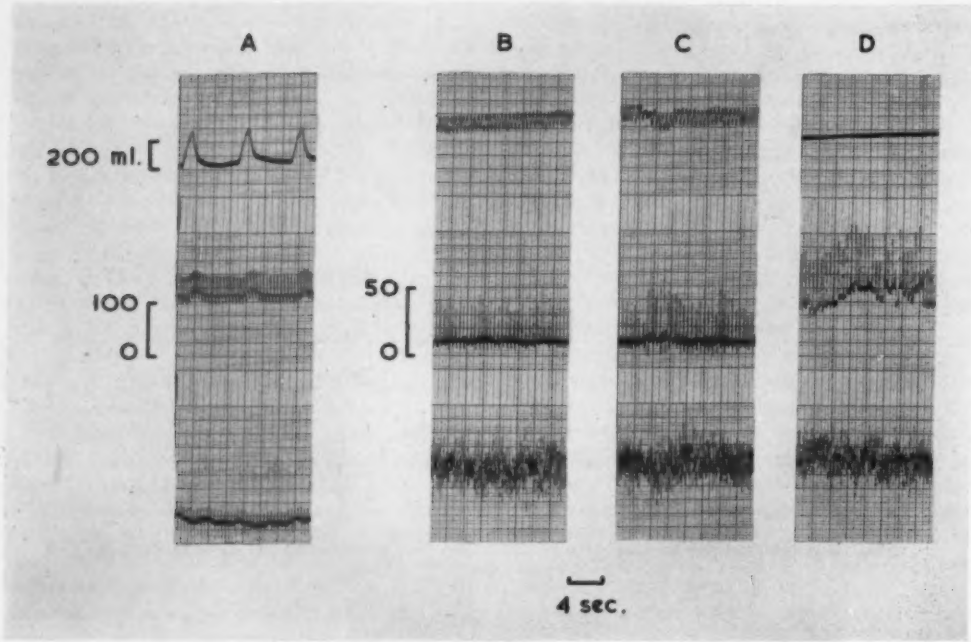

FIG. 2

Respiratory exchange (upper tracing: measured by an integrated pneumatograph attached to the end of an endotracheal tube), blood pressure (middle tracing: note change of calibration between A and B), and (bottom tracing) electrocardiogram of an anaesthetized dog. In A, the control record, the dog was breathing spontaneously: the blood pressure was 150/100 mm Hg and the tidal volume about 250 ml, at a rate of 10 breaths/min. Ventricular fibrillation was then induced by the external application of an alternating current. B is the record obtained shortly after the onset of ventricular fibrillation, after spontaneous respiration had ceased. The dog had been placed on a soft foam rubber mattress and open-chested massage commenced at a rate of about 120/min to imitate the control heart rate. This produced a blood pressure of about 40–45/10 mm Hg. The respiratory exchange was over 10 litres/min. The foam rubber mattress was then removed and open-chested massage continued, the dog now lying on a firm wooden table. This slightly raised the efficiency of the massage, systolic blood pressure increasing, in some beats, to above 50 mm Hg. Between C and D the chest was opened, and D is the record obtained on manual cardiac massage with the pericardium unopened. A pressure of 80–90/40–50 mm Hg was now obtained. There was now, of course, no respiratory exchange. It is to be noted that the scaphoid shape of the dog's thorax makes close-chested massage less effective than in human beings, especially children. The effectiveness of the direct cardiac massage in this instance is exaggerated by the increased development of asphyxia between C and D.

on the chest or even sudden displacement of the heart against the chest wall may give a mechanical stimulus which can restore a normal beat after asystole: in those instances where no defibrillation is needed for normal resumption of the circulation, this is likely to be the case and may have been the explanation for at least several of the successes reported by Rainer and Bullough. Furthermore, the latter recommend chest-squeezing 12–15 times, while Kouwenhoven and co-workers have shown that a satisfactory arterial blood-pressure (systolic levels of up to 80–100 mm Hg) can be achieved only by very forceful rapid compression (not slow squeezing) at a rate of about 80/min. It is, however, possible that the method of Rainer and Bullough is sufficient to supply the "residual circulation" whose importance has already been discussed. Further experimental evidence on the

effectiveness of their method is required before it can be assumed to provide a substitute for the external cardiac massage demonstrated by Kouwenhoven and co-workers.

The second aspect, the provision of an adequate oxygen supply to the blood in practice implies the application of artificial ventilation, since satisfactory spontaneous respiration will generally have ceased shortly after the circulation has stopped. Here, again, the last few years have seen a great advance in the demonstration of the effectiveness of expired-air resuscitation (Elam, Brown and Elder, 1954) at a rate and tidal volume which allows the "donor" to provide an adequate gas exchange for prolonged periods without himself being affected (Cox, Woolmer and Thomas, 1960). It is an odd circumstance that this method, which has been known for centuries and empirically found effective by generations of obstetricians and midwives in resuscitating apnoeic new-born babies, should have taken so long to be generally introduced as a first-aid measure while preference has been given to a long succession of other procedures (Fisher, 1944; Mautz and Hosler, 1960).

It is in the essential provision of a normal circulation plus an adequate respiratory minute volume (as long as the airway is unobstructed) that the method of Kouwenhoven is so valuable: one person can in an emergency perform the dual task of providing a "substitute" heart-pump and artificial ventilation.

(2) *Monitors.*

The success of circulatory and respiratory resuscitation can usually be satisfactorily judged by a change of skin colour from cyanosis and the emergence of a palpable pulse. Obviously, the measurement of the blood pressure is desirable as soon as possible. Where a spontaneous and sustained heart beat is not obtained, while resuscitative measures are continued, the registration of an electrocardiogram will give the necessary information about the underlying rhythm. Where drug administration is attempted (e.g., the intravenous injection of procaine amide to terminate paroxysmal ventricular tachycardia), the electrocardiogram is desirable as an indication of conversion to a normal rhythm and a warning sign of toxic effects. Now that closed chest massage has come to be practised there is even less reason than ever previously to delay resuscitative measures until electrocardiographic evidence of the underlying arrhythmia is available. However, the e.c.g. provides evidence of any permanent injury to the myocardium, either sustained before circulatory arrest (perhaps even its cause), or as a result of it and the resuscitative measures (manual direct cardiac massage and electrical defibrillation). As arrhythmias are not infrequent even after successful restoration of cardiac activity, the frequent monitoring of the heart beat with the e.c.g. is important.

An e.e.g. is unlikely to be available at the time of circulatory arrest, unless this occurs during a cardiac operation when it is often registered routinely. But the e.e.g. is of definite prognostic importance following cardiac arrest, since it gives an indication of the likelihood of complete recovery when recorded shortly after the episode, and provides evidence, in serial tracings, of recovery or permanent damage.

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PHARMACOLOGICAL CONSIDERATIONS IN CARDIOVASCULAR RESUSCITATION

BY

D. R. WOOD

Department of Pharmacology, University of Leeds, England

PHARMACOLOGICAL EFFECTS OF TRANSFUSION FLUIDS

Transfusion as part of resuscitation may be required for the replacement of loss of blood or of fluid. Some hazards, such as the possibility of overloading of the circulation, are common to all transfusion procedures. Other potential hazards vary according to the nature of the material to be transfused. Lehane (1961) has drawn attention to some of the precautions needed to prevent transfusion reactions. The present discussion will be limited to that of the pharmacological effects which may result from transfusion of blood, plasma and saline solutions.

Blood.

We are not concerned here with the possible transmission of infection nor with the effects of incompatibility. Particular attention will be devoted to toxic effects of citrate and potassium.

Citrate toxicity.

Blood stored for transfusion usually contains sodium dicitrate and glucose. These additions prevent coagulation, reduce haemolysis and also delay the diffusion of potassium from the red cells into the plasma. In each bottle of blood transfused there will be from 2 to 2.4 g of sodium dicitrate. Under many conditions the presence of this proportion of citrate in transfused blood is unlikely to be of much concern. However, as the volume to be transfused is increased, so the danger of citrate intoxication increases also. Massive blood transfusions may theoretically cause cardiac depression and even tetany or increased tone and irritability of skeletal muscle, due to a reduction in the concentration of ionized calcium in the patient's plasma. However, if liver function is normal, citrate metabolism is quite rapid. It has been shown that the infusion of up to 8 g of sodium citrate within 10 minutes produces no toxic effects. Since even in hypocalcaemic tetany there is rarely any interference with the blood clotting mechanism, the infusion of citrated blood is unlikely to interfere with the coagulability of the blood by any effect on ionized calcium. In the "acute defibrination syndrome" fresh blood rather than stored citrated blood is preferable; in such a condition the need is for fibrinogen, prothrombin and its precursors and platelets. Occasionally stored blood may be so deficient in normal clotting factors and result in such dilution of those already in the patient's circulation, if large volumes are transfused, that a haemorrhagic state may be induced in the patient. This haemorrhagic state clearly is unrelated to citrate excess.

Mollison (1951) calculated that the danger of toxicity due to citrate in blood transfused intravenously, may usually be ignored if the rate of transfusion does not exceed 100 ml of whole citrated blood per kg per hour. This corresponds, in an adult, to a rate of about 5 l./hr (or 12 standard bottles). This rate of transfusion may be approached in exchange transfusions in infants and perhaps in the course of some surgical operation in which massive haemorrhage occurs.

When large transfusions are given directly into the aorta or heart, as in cardiac surgery, citrated blood is likely to be toxic and the blood intended for such use should be freshly drawn using heparin rather than citrate as the anticoagulant.

In concentrated suspensions of red cells (packed cells) the citrate concentration is reduced by about 50 per cent during the preparation of the suspension.

Except when blood is to be transfused directly into the aorta or heart, whole citrated blood is unlikely to give rise to toxic effects due to its

citrate content. The chance of such effects will be increased in the presence of depressed liver function and although cardiac depression may be apparent, neither frank hypocalcaemic tetany nor convulsions are unlikely, especially under general anaesthesia.

The usual recommended treatment for citrate toxicity is the intravenous administration of 10 per cent solution of calcium gluconate. The required dose is of the order of 10 ml for each litre of citrated blood transfused.

Potassium toxicity.

The potassium concentration of stored blood increases with time due to diffusion of potassium from the red cells into the plasma. Any haemolysis will also result in an increase of plasma potassium. Both these events are less likely to occur if the blood is taken with proper precautions into a sodium dicitrate-glucose diluent. Even so, with storage some rise in plasma potassium content may be expected. Normally the serum potassium of a healthy person lies between 4 and 6 m.equiv/litre. Electrocardiographic changes suggestive of cardiac depression may be apparent when the serum potassium attains a level of about 8 m.equiv/l. but are unlikely to be of serious import until this reaches about 10 m.equiv/l. In blood stored for 3 weeks, the potassium concentration of the plasma may reach 30 m.equiv/l., and it is clearly possible that transfusion of such blood could lead to high potassium levels in the patient's blood. The risk of attaining a high enough concentration to cause cardiac depression or arrest depends on the quantity of blood and the speed at which it is given. Even a relatively small amount of blood with a high potassium content may be dangerous if given very rapidly because a toxic serum potassium level may occur before complete mixing and a steady state are reached. Under normal conditions the excess potassium is taken up into cells and later, given good renal function, eliminated in the urine. In hypovolaemic states in association with surgery and general anaesthesia, there may be some temporary renal vasoconstriction but this will usually be reversed when the normal blood volume is restored. The work of de Wardener et al. (1953) suggests that in people with good kidney function any such brief renal ischaemia is unlikely to be significant. However, it is conceivable that in the presence of prolonged hypotension and persistent renal vasoconstriction any excess potassium ion transfused in stored blood may be more slowly eliminated, with great potential danger to the myocardium.

As with citrate, the chance of ill-effects due to potassium is greatly increased if stored blood is used for direct transfusion into the aorta or heart. The potassium-rich stored blood will be carried into the coronary vessels and cardiac arrest may occur. If fresh blood is used this danger is greatly reduced.

If it is anticipated that large volumes of blood may be required for intravenous transfusion in any patient, then fresh blood with a low plasma potassium is to be preferred.

The stress associated with injury, anaesthesia and surgery, will itself initiate well-recognized alterations in fluid and electrolyte balance in the body. These, especially an increase in extracellular potassium occurring during the first 48 hours after operation, are additional reasons for special care in the proper choice of blood for transfusion during the operation.

Pyrogenic reactions.

Febrile reactions to blood transfusion are usually transient and tend to occur late during the infusion or shortly after. The pyrogens responsible may have been present in the diluent solution, or in the donor's plasma, or may have been derived from bacterial contamination of the blood during collection.

Plasma.

Derived from blood collected in citrate-glucose solution, plasma will contain citrate and a variable amount of potassium depending on the length of storage of the blood before processing for extraction of dried plasma. Transfusion of plasma may be indicated in cardiovascular resuscitation when there has been relatively little haemorrhage, or may occasionally be used as a temporary expedient, when severe haemorrhage has occurred, before blood is available. If plasma is used after reconstitution to the normal 400 ml (per standard M.R.C. bottle of dried solids) the possibility of serious citrate or potassium toxicity is practically small, unless very large volumes or very rapid

infusions are to be given, when the problem is similar to that of using stored blood. The volume and rates of infusion commonly used are unlikely to lead to dangerous levels of citrate or potassium in the patient. The risk may be expected to be higher if more concentrated plasma or serum is used, when indicated for particular purposes, since in these preparations the concentrations of citrate and potassium will be correspondingly higher than in normal plasma.

Pyrogenic or allergic reactions to plasma (1 to 3 per cent of all transfusions) may also occur as with whole blood transfusion.

Plasma substitutes.

Synthetic substitutes for plasma, for use as plasma expanders by virtue of their osmotic effects, need no anticoagulant and carry no risk of causing potassium toxicity. The dangerous pharmacological effects of solutions of gelatin or dextran are due to other factors. All may be expected to produce effects associated with haemodilution, particularly minor effects on blood clotting, if large volumes are infused.

The newer preparations of gelatin have been reported to cause minor and temporary renal disorders. The chief side effect of dextran (Intradex, etc.) from this point of view is an increase in bleeding time occasionally found after infusion of 1 litre or more of the usual 6 per cent solution. This effect is probably only partly due to dilution of coagulation factors in the recipient's blood. Allergic reactions, sometimes severe, have been reported to occur during or after 1 to 2 per cent of dextran infusions.

In the present context these plasma expanders may be safely used in limited quantities for replacement of sudden but limited blood loss or as the initial treatment of larger haemorrhages while blood is awaited.

Saline and glucose.

These are, of course, likely to give only temporary benefit as blood volume expanders since they diffuse rapidly from the circulation. They may have a place in the early stages of treatment of cardiovascular collapse if there is delay in obtaining whole blood or plasma. Apart from dangers such as pulmonary oedema associated with too rapid infusions of such solution, the commonest pharmacological effect is a pyrogenic reaction. The incidence of these, presumably due to faulty preparation or technique, is relatively low.

DRUG-INDUCED CARDIAC FAILURE

Beard (1961) has discussed the aetiology of cardiac and peripheral circulatory failure. The factors that may predispose or precipitate failure are many and variable. Such failure may be the resultant of many insults to a normal or diseased cardiovascular or respiratory system. Thus in reviewing the role of drugs as causes of cardiac failure it is vital to consider their actions against a background of cardiorespiratory disease, disturbed fluid or electrolyte balance, improper anaesthetic technique, and various metabolic factors including hypoxia, anaemia and hypercapnia.

Even though a particular anaesthetic such as ether is generally regarded as being safe from the point of view of cardiovascular toxicity, it is well recognized that patients and conditions vary so widely that such generalizations are not always helpful.

Apart from the drugs used in the anaesthetic administration, previous therapy may predispose to cardiac failure. The contributory effect is often one of metabolic disturbance.

Prolonged *adrenocortical hormone treatment* may so depress the activity of the adrenal cortex that it is incapable of the usual response during the stress of anaesthesia and operation. Hypotension and cardiovascular collapse occasionally occur under these circumstances. The pre-operative preparation of such patients involves a careful review of their electrolyte balance and corticosteroid therapy. An attempt can be made to avoid the appearance of a state of relative adrenocortical insufficiency. Even so it is wise for the anaesthetist to have available an injectable preparation of hydrocortisone for immediate use if required during the operation.

In *thyroid disease* it is desirable that the patient should be adequately prepared. Unsatisfactory control of either hyper- or hypothyroidism may predispose to cardiovascular collapse. The inexpert use of antithyroid drugs in hyperthyroidism may produce a hypothyroid state which will influence the relative safety of anaesthetic agents.

The possible dangerous cardiovascular effects of anaesthetics and other central depressants may be

increased in patients whose *liver function* has been significantly depressed by previous drug treatment.

It is obviously impossible to consider here all the drugs which might predispose to cardiac failure during anaesthesia. From these few examples it will be clear that drugs other than those used by the anaesthetist may play a very significant role in determining the incidence of cardiovascular collapse. To these should be added some of the *adjuvant drugs* used by the anaesthetist himself. In this category are included such classes of drugs as muscle relaxants, morphine, pethidine and similar narcotics, the chlorpromazine-promethazine group, and ganglion-blocking drugs.

Any procedure, including the use of drugs, which increases the risk of hypoxia, hypercapnia, diminishing venous return or direct myocardial depression, will facilitate or potentiate the possible toxicity of the anaesthetic agent. It appears, then, that drugs other than the anaesthetic may be of crucial importance as contributory causes of cardiac failure since they may influence critically the relative cardiovascular toxicity of the anaesthetic on the particular patient under the specific conditions at the time. This conclusion emphasizes again the "experimental" aspect of each individual administration of an anaesthetic.

DRUGS USED IN RESUSCITATION WHICH AFFECT THE FUNCTION OF THE HEART

"The term cardiac resuscitation applies to that action taken to save the life of a patient whose heart has suddenly ceased to beat . . ." (Turk and Glenn, 1954). In cardiac resuscitation the situation is urgent even if, occasionally, expected.

As in resuscitation of a patient with respiratory arrest, so in cardiac resuscitation it is unwise to depend on some drug to restore functional activity. In cardiac resuscitation the essential need is that "oxygenated blood must be artificially propelled to the nervous system" (Stephenson, 1958). Whether the condition is one of cardiac standstill or of ventricular fibrillation, the effect is the same; no blood moves out of the heart. Immediate steps are to initiate or continue artificial respiration with oxygen (there is no point in using anything other than 100 per cent oxygen at this stage), and to begin cardiac massage.

The use of drugs comes later, either to assist returning cardiac contractions or with the hope of initiating them if the heart has not begun to beat spontaneously.

For any treatment to be effective there must be adequate coronary flow of oxygenated blood. Massage alone will not be sufficient if input of blood to the heart is inadequate. This is an indication for transfusion, perhaps into the aorta or heart itself, perhaps intravenously, and some benefit may follow compression of the aorta either just below the origin of the great vessels or even in the abdomen. Massage may be life-saving.

Some authorities recommend injection of, for example, adrenaline with procaine through the unopened chest as an initial procedure which may make thoracotomy unnecessary. Undoubtedly this manoeuvre occasionally stimulates a return of spontaneous beats. However, it leaves too much to chance and is regarded by many as being dangerous because it wastes precious time. When it does restore cardiac contractions, this procedure is more likely to have been effective because of the mechanical stimulus than as a result of any action of the drug injected into an anoxic heart. On occasion, it may be doubtful whether cardiac arrest has occurred and it may be justifiable in such cases to give an intravenous injection of, for example, noradrenaline (50–75 μg) with massage of the vein towards the heart (Churchill-Davidson, 1956). If the heart is still beating, this will raise the blood pressure and restore a peripheral pulse. The effect is primarily due to peripheral vasoconstriction. On the other hand, considering that the time available for adequate treatment of cardiac arrest is so short, others feel that thoracotomy is justifiable even if, occasionally, the heart is found to be still beating on opening the chest. Stephenson (1958) reports such a finding in 6 patients out of 1,710 reviewed. Turk and Glenn (1954) found the heart beating in 2 of 42 patients after performing thoracotomy for cardiac arrest.

DRUGS USED FOLLOWING CARDIAC MASSAGE AFTER CARDIAC STANDSTILL

Calcium chloride, barium chloride, adrenaline, isoprenaline and other sympathomimetic amines are among the drugs advocated by different authorities.

Calcium chloride.

An increase of extracellular calcium causes an increase in contractile force of isolated mammalian heart muscle but has little effect on automaticity. It produces a moderate increase in the threshold of irritability. Effects of calcium in cardiac automaticity in the whole animal may be secondary effects following the release of catecholamines from the adrenal medulla.

The restoration of cardiac contractions by injection of calcium chloride was recommended by Kay and Blalock (1951). It causes an increased tone and contractibility of heart muscle. They recommend use of 10 per cent calcium chloride solution in a dose of 2 or 3 ml. Others (Beck, 1956) use 0.5 ml of a 1 per cent solution.

Barium chloride.

Barium increases the irritability of the ventricles and strengthens contractions. There have been several reports of the usefulness of barium chloride injections in cardiac resuscitation. Many would consider it to be less successful than calcium and potentially more dangerous because its effect on irritability may more easily lead to arrhythmias including fibrillation. Although Stephenson (1958) claims that he has been more impressed with the beneficial effects of barium chloride, others condemn it as being "a dangerous and unreliable drug . . ." (Nalefski, Gilbert and Fenn, 1950).

Adrenaline.

This is still widely used in attempts to restore the activity of the arrested heart. Everyone who has seen the effect of adrenaline on an isolated perfused mammalian heart cannot fail to be impressed by its powerful effects on cardiac contractions under those conditions. It certainly increases the force of contraction and the rate of the heart but also may cause extrasystoles and fibrillation. It increases the metabolism of the heart and in spite of an increase in absolute coronary flow there may be a relative coronary insufficiency. In practice this implies that although under favourable conditions, adrenaline may be effective in restarting the heart, it may also provoke ventricular fibrillation. Attempts have been made to increase the safety of adrenaline by using it together with procaine. Because of its quinidine-like action, procaine might be expected to diminish the possibility of cardiac arrhythmias due to adrenaline. However, the use of adrenaline with procaine for this purpose has not commanded wide support. It is difficult to assess the relative value of this modification since controlled trials are, not surprisingly, lacking (Laurence and Moulton, 1960).

Isoprenaline and other sympathomimetic amines.

Theoretically, and supported by some experimental and clinical evidence, it might be expected that other sympathomimetic drugs would have advantages over adrenaline in restoring cardiac function.

Nathanson and Miller (1952) compared the effectiveness of adrenaline, noradrenaline and isoprenaline in preventing or abolishing cardiac standstill produced in man by carotid occlusion. The drugs were injected intravenously. Noradrenaline was ineffective but isoprenaline was more active than adrenaline and did not produce ectopic ventricular beats. Other evidence would also suggest that isoprenaline might be preferable to adrenaline from this point of view. Orth, Stutzman and Meek (1944) showed that isoprenaline was much less likely to cause ventricular arrhythmias during cyclopropane and other forms of anaesthesia. However, as with adrenaline, isoprenaline may induce a relative coronary insufficiency. It must also be remembered that the peripheral actions of isoprenaline are likely to lead to a fall in blood pressure and a reduction in coronary flow. Phenylephrine (Neosynephrine), ephedrine, and other sympathomimetic agents, affect especially the peripheral vessels rather than the heart. They are not suitable for a direct cardiac action in treatment of cardiac arrest.

It is probably true that the possibility of ventricular arrhythmias is present when any of the sympathomimetic amines is used. This is the major drawback to their use in cardiac resuscitation.

The supposed "cardiac stimulants" such as leptazol (Cardiazol) and niketharnide (Coramine) are quite valueless as specific remedies for direct action on the heart. Any beneficial effect they may produce under other circumstances of peripheral circulatory failure is probably due to their central stimulant action, thus increasing vasomotor tone and secondarily improving cardiac output.

Digitalis glycosides are contra-indicated. Their relatively slow onset but prolonged duration of action makes them unsuitable in this type of emergency, quite apart from the complications that their presence would introduce if other therapy were then to be attempted after unsuccessful use of digitalis.

The usefulness of calcium chloride, adrenaline or isoprenaline after cardiac massage clearly depends on the drugs reaching a myocardium which is able to respond. The drug must pass into the coronary arteries and thence to heart muscle which is receiving oxygenated blood. Injection into the blood within a ventricle is indicated and although there is argument about whether the injection should be made into the right or left ventricle, it would seem logical to prefer the left ventricle. The drug will reach the coronary vessels more rapidly. The injection of such a drug should be secondary to cardiac massage, with transfusion if required.

DRUGS USED AFTER ELECTIVE CARDIAC ARREST

With a heart-lung machine to by-pass the heart it is now possible to stop cardiac activity by elective injection of potassium salts. Potassium citrate or potassium chloride are the salts commonly used for this purpose.

It is generally expected that normal cardiac activity will return spontaneously when the potassium is flushed out by oxygenated blood after completion of the operation. Instead there may be ventricular fibrillation or heart block. Fibrillation may precede normal rhythm or may persist. Electrical defibrillation or a second arrest by potassium citrate may be followed by restoration of normal rhythm. Cautious use of isoprenaline may be effective in increasing the ventricular rate during temporary heart block. Cardiac massage is obviously better avoided and experience of using calcium chloride or adrenaline has not been successful.

DRUGS USED FOR VENTRICULAR FIBRILLATION

When ventricular fibrillation is the cause of acute cardiac failure, occurring primarily or during attempts to resuscitate the arrested heart, cardiac massage, if not already tried, and electrical defibrillation are indicated. The use of drugs may be essential if an electrical defibrillator is not available. Several possibilities may be considered. Potassium citrate or chloride (10 per cent) may be injected to cause cardiac arrest, with the hope that spontaneous rhythm may return after further cardiac massage or the subsequent injection of calcium chloride or isoprenaline solution.

Earlier enthusiasm for use of procaine or its longer-acting derivative, procaine amide, in treating ventricular fibrillation has not been borne out by further experience, although the exact status of these drugs is still undecided.

The rational basis for using procaine applies equally to quinidine and other drugs with a quinidine-like action. Procaine and procaine amide may be relatively safer, but all have the practical disadvantage that they cannot be relied on.

Stephenson (1958) reports that Harken finds that standstill caused by procaine or potassium chloride, followed by massage and calcium chloride, is most effective. Other reports indicate that electrical defibrillation may be more successful after an injection of procaine or procaine amide, but this is not universally agreed. The prolonged depression of cardiac contractility which is produced by potassium salts may make it difficult to restart the heart, although it is very effective in stopping fibrillation.

Adrenaline would appear to be contra-indicated because of its known propensity to increase cardiac excitability. It is occasionally reported to have been successful in restoring a normal rhythm (Milstein, 1956).

As already implied, the status of drug treatment of ventricular fibrillation is still uncertain and more reliance has come to be placed on electrical defibrillation (Milstein, 1961).

DRUGS USED IN RESUSCITATION FOR AN EFFECT ON PERIPHERAL VESSELS

Acute peripheral circulatory failure may result from a reduction in blood volume or loss of vasomotor function (Greisman, 1959). Some of the causes contributing to the loss of vasomotor function, including an inadequate airway, too much anaesthetic, and mechanical interference with venous return to the heart, can be dealt with by the obvious treatment. Provided that the heart is still beating and the circulating blood volume is adequate, attention to oxygenation and the

injection of a vasoconstrictor drug may restore a more normal blood pressure.

The requirement for *oxygen* is dictated by the need to relieve anoxaemia as a possible cause of peripheral vasodilatation. The *pressor drug* should produce its effect by causing peripheral vasoconstriction only. The action should be prompt, predictable and controlled and not accompanied by any cardiac stimulation. A drug like adrenaline which also stimulates the heart directly is unsuitable because it may produce a relative coronary insufficiency. The induced myocardial stimulation and increase in oxygen consumption may not be met by any increase in coronary flow. It is also desirable that the drug does not cause hyperirritability of the ventricle which may lead to arrhythmias including fibrillation.

Noradrenaline (Levophed, Adrenor) is perhaps the most commonly used peripheral vasoconstrictor in these circumstances. Its use in doubtful cases of cardiac arrest has already been mentioned. A more definite indication is as a single injection or as a continuous intravenous infusion to restore a low blood pressure. Unlike adrenaline it causes a generalized constriction of small vessels—arterioles and precapillaries. Systolic and diastolic pressures rise and coronary blood flow is increased. The direct stimulant effect of noradrenaline on the heart is very much less than that of adrenaline and is usually more than overcome by the reflex vagal slowing induced by the rise in blood pressure. It is much less likely than adrenaline to cause ventricular fibrillation. The renal blood flow may be temporarily reduced following the injection, but unless large doses or infusion rates are given the increase in arterial pressure compensates for the renal vasoconstriction and renal function is restored. The B.P.C. injection of noradrenaline contains 2 mg of the acid tartrate per ml. This is diluted with normal saline or glucose solution to 250 times its volume. The dilute solution contains 8 μg/ml and is infused at a rate determined in each case by the effect on the blood pressure, usually between 2 and 4 μg/min.

Other sympathomimetic amines with similar effects are phenylephrine, mephentermine and methoxamine. All three drugs are vasoconstrictors, with little direct effect on the heart or central nervous system. Their duration of action is longer than that of noradrenaline and so they are probably of less use by infusion because their effects cannot be so quickly altered by changing the infusion rate.

Other sympathomimetic agents like ephedrine and methamphetamine (Methedrine) will also raise the blood pressure. In addition to peripheral vasoconstriction, these drugs cause cardiac and central nervous stimulation. Although they have a place in the prevention and treatment of hypotension during spinal anaesthesia, they are less generally useful in other cases of peripheral circulatory failure.

Under the conditions of circulatory failure associated with anaesthesia, vasoconstrictor drugs have a very useful role in restoring an adequate blood pressure to sustain coronary and cerebral blood flow, and may be life-saving. Their action may be regarded as reinforcing the normal compensatory mechanisms which attempt to maintain the systemic blood pressure and blood supply to essential organs. However, as failure progresses it may become irreversible. Capillary function is seriously impaired and loses its responsiveness to noradrenaline. Persistent arteriolar constriction at this time may be expected to contribute to further ischaemia and pooling of blood in the periphery.

Although substances like ganglion-blocking and adrenergic-blocking drugs have some use in preventing haemorrhagic or traumatic shock, by reducing arteriolar constriction, they are generally contra-indicated in the treatment of early or established peripheral circulatory failure.

In the absence of adrenocortical insufficiency it seems unlikely that injection of adrenal corticoids such as hydrocortisone will enhance the cardiovascular response to noradrenaline although this is known to occur under normal conditions in man.

GENERAL CONSIDERATIONS

In the prevention of, and prophylaxis against, cardiovascular emergencies during anaesthesia, a number of factors, some obvious, require emphasis. The prevention of carbon dioxide accumulation, adequate oxygenation and atropinization will help materially in diminishing the chance of failure from anaesthetic causes. Careful consideration of any drug treatment which the patient has been

receiving may also limit the incidence of such emergencies, if appropriate measures are taken before operation. Such knowledge may also be important in determining the actual treatment of any cardiovascular emergency. Adrenocortical hormone therapy, drugs such as diuretics which may modify electrolyte balance and others used in the treatment of hypertension are among those which may profoundly alter the incidence and prognosis of such emergencies.

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CARDIAC RESUSCITATION

BY

B. B. MILSTEIN
Thoracic Surgical Unit, Papworth Hall, Papworth, Cambridge, England

Historical review.

The earliest record of an attempt to resuscitate the arrested heart is found in the works of Vesalius, who used artificial respiration (Willius and Dry, 1948). Similar experiments were made by John Hunter, who performed tracheotomy on animals and introduced bellows into the trachea for artificial respiration. By stopping the action of the bellows he produced cardiac asystole. He showed that when artificial respiration was begun again within ten minutes the heart would often recover. He concluded "It appears that anything salutary to life applied to the lungs would restore the heart's action after it had been at rest for some time" (Hunter, 1776).

Harvey, too, had observed resuscitation of the heart. In "De Mortu Cordis" he referred to an experiment in which the arrested heart of a pigeon began to beat again after he had stimulated it with the contact of a warm finger.

The greatest advances in the treatment of cardiac arrest were made by Moritz Schiff, professor of physiology at Geneva (fig. 1). His experiments were carried out in 1874, and were published in his collected works (Schiff, 1896). His interest was initially in the cause of death from chloroform and ether. He found that compression of the chest, the application of electric currents to the heart, and artificial respiration were unsuccessful in restoring the heart beat. There followed the first description of cardiac massage. Simply, "One makes rhythmic compressions of the heart with the hand, so as to squeeze out the blood". Schiff made it clear that the response of the heart was not due to mechanical stimulation but to the effect of the artificial coronary circulation which resulted from cardiac compression. He also suggested clamping the abdominal aorta in order to increase the peripheral resistance, a technique which was revived by Wiggers (1940b) who advised clamping the thoracic aorta. He demonstrated resuscitation of the heart after as much as 11½ minutes of arrest and described assistance of the circulation by further massage after the heart had recovered but was beating feebly. Schiff's technique for resuscitating animal hearts differs little from the treatment of cardiac arrest in man today.

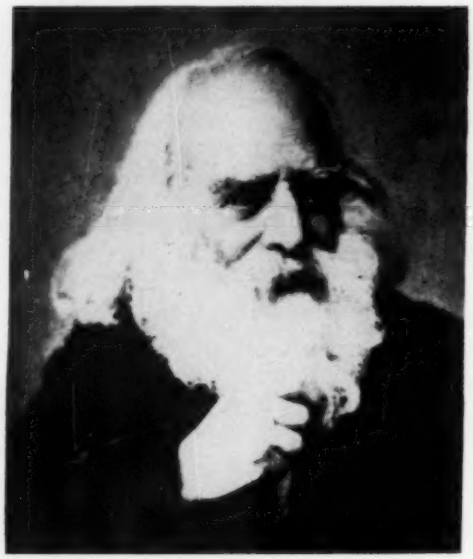

FIG. 1
Moritz Schiff, who described cardiac massage in 1874.

Ventricular fibrillation was first described in 1850 (Hoffa and Ludwig, 1850). Fifty years later Prévost and Batelli demonstrated electrical defibrillation of the heart. They showed that if a shock was applied to the heart within 15 seconds of the induction of ventricular fibrillation, normal rhythm could be restored, but that after a longer interval prolonged massage was first necessary

before defibrillation could be achieved (Prévost and Batelli, 1899, 1900). The proof that ventricular fibrillation was the mechanism of sudden cardiac failure under chloroform anaesthesia was provided by Levy in 1911.

The first comprehensive account of cardiac resuscitation was given by D'Halluin in his book published in 1904. D'Halluin's contributions included the measurement of the blood pressure during cardiac massage for the first time. He also developed a biochemical method for reversing ventricular fibrillation, making use of Ringer's demonstration of the antagonism between potassium and calcium in their effects on myocardial contractility. He treated ventricular fibrillation by the intravenous infusion of 5 per cent potassium chloride. If this diminished the myocardial tone, he gave intra-arterial Locke's solution. If the ventricular fibrillation persisted, 5 per cent calcium chloride was injected intravenously. This is the basis of the Melrose technique for induced potassium arrest (Melrose et al., 1955). The use of procaine for reversing ventricular fibrillation had been studied by Beck in 1937 and was used clinically by him in 1941. A defibrillator for clinical use was developed by Hooker, Kouwenhoven and Langworthy (1933), and was successfully used on a dog heart, but it was not used with success in man until 1947. Much of our knowledge of the physiology of ventricular fibrillation comes from the researches of Wiggers (1940a) who developed the method of serial defibrillation which will be described later. Hooker and his colleagues had experimented with the use of an external defibrillator which could be applied to the unopened chest, but with little success. The successful use of this apparatus was described by Gurvich and Yuniev (1947) who experimented with it on dogs.

Cardiac resuscitation in man.

Attempts to treat cardiac arrest in man by cardiac massage were made towards the end of the nineteenth century. The first of these was by Niehaus of Berne, probably in 1899 (Zesas, 1903). There was a long delay before the chest was opened and no response could be obtained from the heart. The pioneer French surgeon Tuffier reported the case of a man of 24 who collapsed in the ward a few days after an operation. He made an intercostal incision and compressed the ventricles for one to two minutes. The heart began to contract and the pupils became normal in size. Subsequently the pulse disappeared and the heart failed to respond to further treatment. This was not surprising for the patient had suffered a massive pulmonary embolus (Tuffier and Hallion, 1899). Many other unsuccessful examples were reported. The first successful cardiac resuscitation was by Igelsrud in 1901 (Keen, 1904). Cardiac arrest occurred after a hysterectomy. "The heart was laid bare by a resection of parts of the fourth and fifth ribs, the pericardium was opened and the heart massaged between the thumb on one side and the fore and middle fingers on the other. Pulsations returned after one minute." The patient recovered completely. The first success in man to be reported was by Arbuthnot Lane (Starling and Lane, 1902). Pulse and respirations ceased during an operation for the division of peritoneal adhesions under ether anaesthesia. The heart started after subdiaphragmatic compression. In 1906 Green collected forty published examples of attempted cardiac resuscitation, with nine recoveries. Many series have been published since that time, but the success rate has remained at between 25 and 30 per cent.

The first recovery after *electrical* defibrillation of the heart was reported in 1947 (Beck, Pritchard and Feil, 1947). Before this, defibrillation of the human heart by the use of *procaine* had been reported by Adams and Hand (1942). Up to 1954 only eighteen recoveries from ventricular fibrillation had been reported. In that year a series of thirty instances of ventricular fibrillation occurring during cardiac operations was reported. Defibrillation was achieved in twenty of these and nine of the patients recovered completely (Milstein and Brock, 1954).

The problems of delay before starting cardiac resuscitation is still unsolved. Stephenson (1958) collected a series of 1,710 patients who had cardiac massage—most of them within recent years—and found that the mortality rate was 71 per cent. Fear of opening the chest, delay in diagnosis and ignorance of the proper procedure are the causes of this high mortality.

With the great expansion of cardiac surgery in recent years treatment of cardiac arrest has

become more widely known. For certain special circumstances methods such as the use of an external pace-maker and an external defibrillator have become available and the heart can be stimulated with internal pace-makers by many different means. Many successful resuscitations of patients who have suffered myocardial infarction have been reported (Beck, Weckesser and Barry, 1956). The greatest advance made since the time of Schiff is the demonstration that cardiac massage can be carried out effectively through the closed chest (Kouwenhoven, Jude, and Knickerbocker, 1960). This method is just as effective as open chest cardiac massage. It has the advantage that no thoracic incision is required and no special apparatus is necessary. It can therefore be carried out immediately, even by untrained personnel. It is to be hoped that as a result of this simple technique, cardiac massage will be carried out in the future without delay. In this way the present high mortality of 70 per cent can be reduced to 10 per cent or even less.

Treatment of cardiac arrest.

The immediate treatment for cardiac arrest is to restore the supply of oxygenated blood to the brain. Serious cerebral damage or death is inevitable if this is not done within three minutes. Cardiac compression provides an adequate artificial circulation. At the same time a clear airway must be established and the lungs ventilated with oxygen. The emergency is thus overcome, and the heart can be restarted at leisure.

Restoration of the circulation of oxygenated blood to the brain in this short period is not possible unless a pre-arranged plan for dealing with such an emergency has been established. Cardiac arrest must be dealt with by the first person to reach the patient, without waiting for assistance to arrive. He therefore must be fully trained in the technique of resuscitation. The essential equipment must be accessible in a central situation known to every worker. Every hospital should also have an alarm system specifically for patients who suddenly collapse, so that help can be summoned quickly. Normal methods of hospital communication such as the telephone are unsuitable for alarm purposes because delay may occur. A system of bell pushes in strategic places, alarm bells and indicators can be installed very cheaply. The alarm is answered by every available doctor and the first ones to appear on the scene provide the treatment. When the alarm sounds a trolley of resuscitation equipment is taken from its store to the site of the emergency according to a pre-arranged plan.

Frequent instruction in the drill for cardiac resuscitation must be given to hospital staff. This must include lectures, demonstrations of the technique of cardiac massage and of the resuscitation equipment and its use. In an emergency, nurses, technicians and porters may be required to give assistance, so that they must also receive some training if mistakes are to be avoided.

Immediate treatment.

The patient's head should be lowered and the legs elevated. This increases the blood pressure in the cerebral vessels and improves the venous return to the heart. At the same time several vigorous thumps should be given to the precordium. This manoeuvre can restore the beat when cardiac asystole is present (Scherf and Bornemann, 1960). Ventilation of the lungs must be established simultaneously. Initially this will be by mouth-to-mouth or mouth-to-airway respiration with expired air. At a convenient time a facepiece and breathing bag may be substituted. An endotracheal tube is not essential. The inexperienced should not attempt to introduce one because their efforts may only result in increased anoxia.

Percussion of the precordium and elevation of the limbs should occupy no more than fifteen seconds. The insertion of needles into the heart is inadvisable, for this may cause cardiac tamponade. If these manoeuvres are successful, the pulse will return, the pupils constrict and colour will return to the face. In the absence of an obvious recovery of the circulation, external cardiac massage must be started immediately, and assistance must be sought. The operator must also send for ventilation apparatus, a knife, a defibrillator and an electrocardiograph.

External cardiac massage.

This technique was developed by Kouwenhoven, Jude and Knickerbocker (1960). Compression of the heart between the sternum and the spine forces blood out into the systemic cir-

culation. Lateral displacement is prevented by the pericardium. One would imagine that this method is only suitable for the elastic thorax of the child, but it has been shown that it is equally effective in unconscious patients of any age. The patient lies supine on a rigid surface. One hand is placed over the lower end of the sternum and the other pressed vertically downwards over it 60 times a minute. The sternum should be displaced 3 to 4 cm towards the spine. This requires the operator to use his body weight in addition to his shoulder muscles (fig. 2). The hands are relaxed completely after each compression. In this way a systolic blood pressure of up to 100 mm Hg can be generated. Ventilation of the lungs must also be performed, for the gaseous exchange resulting from sternal compression is quite inadequate. Until assistance is available the cardiac massage must be interrupted every minute while the operator ventilates the lungs with a few breaths by mouth-to-mouth insufflation.

This technique of cardiac massage is now the method of choice for the treatment of cardiac arrest. The suggestion that it is only suitable for "non-surgical" patients with cardiac arrest is quite incorrect. Direct cardiac massage will of course be carried out when the chest is already open, and in certain special circumstances. We have treated seven patients by external cardiac massage, six of them successfully. One patient was treated by a staff nurse without any assistance. This technique has transformed a major surgical emergency into a simple procedure for which no apparatus is necessary. There can now be no excuse for any doctor to fail to treat cardiac arrest immediately in any circumstances.

External cardiac massage is contra-indicated in many cardiac surgical patients, and when cardiac arrest is caused by massive haemorrhage, cardiac tamponade or air embolism. In cardiac surgical conditions, relief of an obstruction or closure of a shunt may be necessary before the heart can regain its beat, and therefore the chest should be opened. The rapid transfusion of blood in the

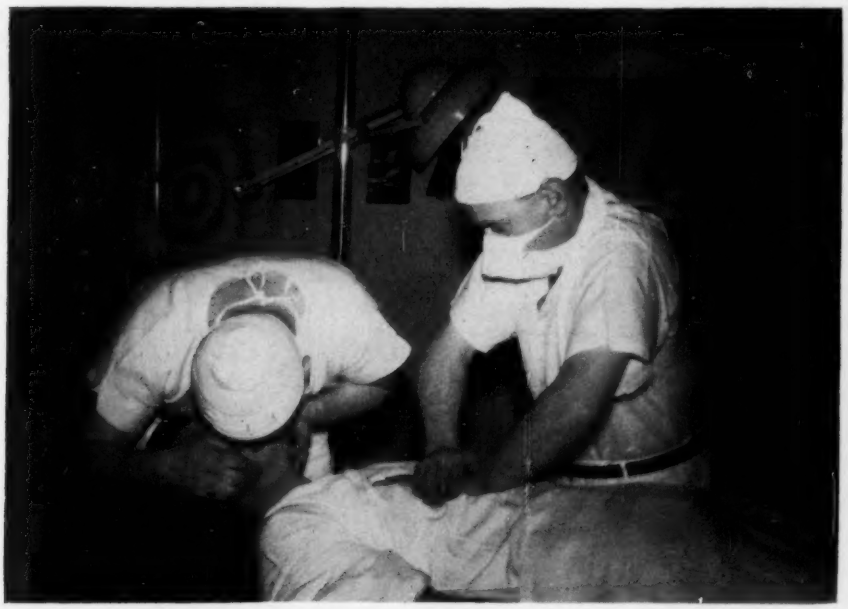

FIG. 2

External cardiac massage and mouth-to-mouth ventilation. Note the position of the operator's hand over the lower end of the sternum and the use of his body weight.

case of haemorrhage can best be achieved by its injection into the heart or aorta. Aspiration of the pericardium is an inefficient and often unsuccessful method of dealing with cardiac tamponade causing cardiac arrest; the pericardium should be opened to relieve the tension and direct cardiac massage performed. When the right ventricle is filled with froth from air embolism, the air must be aspirated before the heart is massaged, and this should be done by exposing the ventricle.

Rib fractures may occur from the force of compression during external cardiac massage, especially in the elderly. They are of little importance if the patient's life is saved by the treatment, but their possible occurrence must be realized so that their complications, such as haemothorax, pneumothorax and surgical emphysema can be recognized and treated.

Another complication of external cardiac massage is tension pneumothorax from rupture of alveoli or bullae. This is only likely to happen if the chest is compressed at the same moment as the lungs are inflated, when very high intrapulmonary pressures can develop. The operator ventilating the lungs should therefore time his inflation to coincide with the period of artificial diastole.

Restoration of the heart action during closed chest cardiac massage.

The methods for restoring the heart beat during direct cardiac massage can also be used in patients undergoing external cardiac massage. Pharmacological agents can be given intravenously because there is an adequate artificial circulation. If ventricular fibrillation is present an external defibrillator can be applied to the chest wall.

An electrocardiograph must be connected to the patient as soon as possible for this is the only means of diagnosing ventricular fibrillation. The electrocardiogram cannot be used for the diagnosis of cardiac asystole, for in this condition electrical activity of the heart may persist for a long time (fig. 3). If asystole persists and an external pacemaker is available, the condition can be dealt with without opening the chest.

Indications for thoracotomy.

Some of these have already been discussed, but in addition external cardiac massage should be abandoned and the chest opened: (*a*) to treat ventricular fibrillation when no external defibrillator is available, or (*b*) if the external massage is ineffective as shown by absence of a carotid pulse and failure of the pupils to constrict.

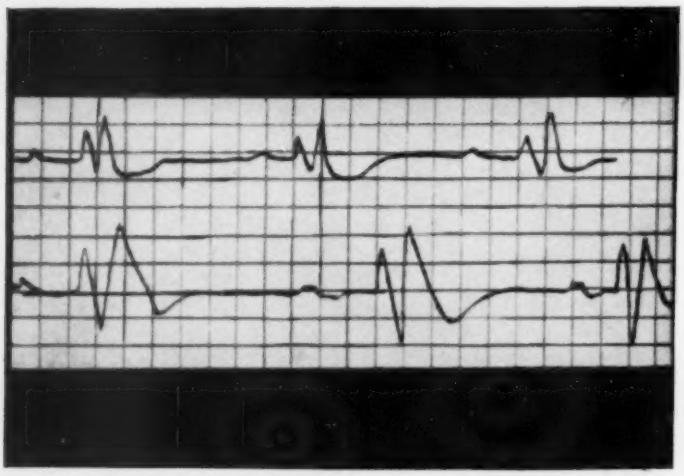

FIG. 3

This e.c.g. tracing, showing recognizable P waves and QRS complexes, was obtained from a heart which had failed to beat spontaneously for two hours.

The commonest causes of failure to resuscitate the patient are inadequate ventilation, obstruction of the airway and improper performance of chest compression. External cardiac massage is quite useless if the patient is lying on a soft bed, which yields with each compression stroke. The patient should be removed from the bed and placed on the floor.

Direct cardiac massage.

The approach should be transthoracic. The alternative routes — transdiaphragmatic, transpleural, subdiaphragmatic—all have serious disadvantages. A sufficiently large incision to admit both hands cannot be made. The heart cannot be seen easily so that it is difficult to differentiate fibrillation from asystole, and injections cannot be made into specific chambers because they cannot be identified. It may also be difficult to place defibrillator electrodes in the correct position.

If an abdominal operation is in progress when cardiac arrest occurs, it is reasonable to compress the heart a few times from beneath the diaphragm with counter-pressure over the sternum, for this method is occasionally successful, but time must not be wasted in persisting with inefficient massage by this route.

Occasionally the presence of gross disease of the left pleura makes transthoracic cardiac massage impossible, and external cardiac massage must be used.

Technique of thoracotomy.

No time must be wasted in following aseptic ritual. There is no time to wash the hands or to obtain sterile instruments. An intercostal incision is made in the left 4th, 5th or 6th intercostal space. This incision must be as long as possible; if it is found that both hands cannot be introduced into the pleural cavity the only reason is that the incision is too short. Care must be used in incising the deepest intercostal muscle fibres so as to avoid injuring the underlying lung.

The intercostal incision is extended backwards as far as the vertebral transverse process. The edges of the incision are forcibly retracted; rib fractures can be ignored. The heart is immediately compressed with one hand, using counter-pressure over the sternum with the other.

Although the operation sounds a formidable one, it has been successfully performed by operators untrained in surgery, such as anaesthetists and cardiologists. Nevertheless, all doctors should practise the operation in the postmortem room so as to become familiar with it. They will then avoid such accidents as incision of the aorta or a coronary artery, or incising into a ventricular cavity. An expert can be massaging the heart within thirty seconds of making the skin incision. A novice should therefore be able to do this well within the available period of three minutes.

Technique of cardiac compression.

As soon as cardiac massage has begun, the situation is under control and the emergency no longer exists, for oxygenated blood is again circulating through the brain. Often the heart beat will return after a few compressions. If it does not do so within thirty seconds the pericardium should be opened. A fold of pericardium is picked up with toothed forceps and nicked with scissors. In this way damage to the heart is avoided. Air is allowed to enter and then the incision is extended along the whole length of the sac anterior to the phrenic nerve. Both hands are inserted through this opening and the ventricles compressed between them. A fairly firm squeeze is required. Too little force will not produce an adequate flow; too much will damage the muscle. Between compressions the hands are relaxed and the heart allowed to fill with blood.

The heart should be compressed between the palms of the hands. If the finger tips are used there is a danger of rupture of the myocardium (Hurwitt and Seidenberg, 1953; Stahlgren and Angelchick, 1960). In massaging very small hearts, when only one hand can be used, counterpressure should be with the thenar eminence and not with the thumb. A further danger is a tear of the junction of the right atrium and inferior vena cava. This is the result of traction on the heart each time it is compressed. A conscious effort must be made to avoid this mistake.

The rate of massage is a matter for controversy. Johnson and Kirby (1949) showed in dogs that the blood flow increased in proportion to the rate of cardiac compression up to a rate of 120 times a minute. In man, increasing the rate sometimes improves the blood pressure but may cause it to diminish. A rate of 50–60 times a minute is usually satisfactory (fig. 4). Rapid rates cannot be maintained for more than a few minutes because

the operator's hands become fatigued. The rate is also determined by the need to wait for the heart to fill before compressing it. This diastolic filling can easily be felt by the hands. When the operator becomes fatigued he should allow the assistants to massage the heart in turn so that they can gain experience in the technique.

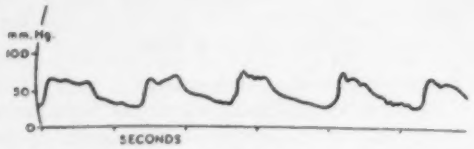

FIG. 4

Electromanometric pressure record during cardiac massage obtained from a needle in a brachial artery. It shows a pressure of 75/30 mm Hg.

Attention may now be given to asepsis and improvement of the exposure. The operators scrub in turn. The skin round the incision is swabbed with antiseptic and sterile towels placed in position. A suitable retractor is inserted. If the massage is effective, the edges of the incision will start to bleed. The divided vessels must be secured, paying special attention to the internal mammary artery.

Cardiac massage properly performed will result in a blood pressure of 50–100 mm Hg. The carotid pulse becomes palpable, the pupils constrict and the skin colour improves. After a time tone returns to the myocardium. An increasing resistance to compression can be felt, and as a result a higher blood pressure can be maintained. The heart is now well oxygenated, and an attempt can be made to restore the natural heart beat. Cardiac massage can be continued if necessary for many hours, and complete recovery has been recorded after continuous massage for eight hours (Hosler, 1953).

Improvement of the cardiac output.

The blood flow during cardiac massage can be improved by measures to increase the venous return and to diminish the size or increase the filling of the vascular bed. The head down position has already been mentioned. Compression of the descending thoracic aorta is a useful way of increasing the blood flow to the cerebral and coronary vessels. The site of compression is just beyond the left subclavian artery. This is not easy to achieve in practice for the aorta is lax and when compressed against the vertebral bodies it tends to slip away from the fingers. The aorta can be mobilized and clamped. The method is a useful one, but neither the expertise nor the instrument is likely to be available. When cardiac arrest has resulted from haemorrhage the heart is empty and massage is ineffectual. Rapid transfusion of blood is required. Intravenous infusion is unsatisfactory, for the impaired heart action implies a slow transference of blood to the arterial system. The blood should be injected intra-arterially. The amount required to restore the blood pressure if this route is used is little more than half the quantity needed when the blood is injected intravenously (Kohlstaedt and Page, 1943).

Blood may be injected into the aorta or into the heart itself (Iokhveds, 1945). Both sites are easily accessible when the chest is open. An intra-aortic injection can be made into the terminal aorta if the abdomen is open. Using a wide bore needle, blood can be infused at 500 ml/min.

An intracardiac infusion is given into the cavity of the left ventricle using a large needle inserted at the apex. Two needles can be used if necessary. The heart can be massaged while the needles are in situ. When the needles are withdrawn the thickness of the ventricular wall prevents bleeding and no suturing is required. When large quantities of blood are infused into the arterial system adequate quantities of calcium gluconate must be given to counteract the adverse effects of hyperpotassaemia on the heart.

Dangers of prolonged massage.

Although cardiac massage can maintain the circulation for many hours, restoration of the heart beat should be attempted as soon as possible, for prolonged cardiac massage may result in myocardial damage. However carefully massage is performed, after a time haemorrhage into the myocardium occurs (Milstein and Brock, 1954). The effect of extensive haemorrhage is likely to be persistent hypotension in the immediate recovery period and late cardiac failure with possibly permanent damage. Subepicardial and subendocardial haematomas may occur, but these are probably of no significance. Sections of the myo-

cardium after cardiac massage has been prolonged show extensive extravasation of red cells into the connective tissue planes and between individual muscle fibres. Adelson (1957) found these changes in 60 per cent of sixty hearts on which cardiac massage had been performed.

Restoration of the heart beat.

As soon as an artificial circulation has been established, consideration must be given to restoration of the heart beat. The treatment to be applied depends on whether cardiac asystole or ventricular fibrillation is present. Asystole is more common, but stimulation of the anoxic myocardium by cardiac massage or by an injection may convert asystole to fibrillation. During open chest cardiac massage observation of the heart will reveal which of these conditions is present, but if external cardiac massage is being performed the differentiation can only be made with the aid of the electrocardiograph. This distinction is of no importance in the emergency treatment of the arrest, for in both states cardiac massage will maintain a circulation. Sometimes the heart beat is quickly restored by massage, but if not the patient must be brought to the electrocardiograph—or the apparatus to the patient.

Before other methods of restoring the heart beat are applied massage must be continued for a sufficient length of time for the whole myocardium to become well oxygenated. This may require five or ten minutes of continuous massage.

Restoration of the heart beat with the chest closed.

The differentiation of cardiac asystole from ventricular fibrillation is made by observation of the electrocardiogram. The treatment of asystole is the injection of 10 ml of 1 per cent calcium chloride solution or 10 ml of 1 in 10,000 adrenaline solution. As there is a peripheral circulation the drugs can be injected intravenously. Alternatively the heart can be stimulated to contract by the application of a small current to the chest wall through an external pace-maker.

If the electrocardiogram shows ventricular fibrillation electric defibrillation of the heart must be carried out. The heart must first be well oxygenated by external massage. If the fibrillation, as seen on the electrocardiogram, remains feeble, an intravenous injection of adrenaline should be given, for this will improve the myocardial tone and make the fibrillation more vigorous (figs. 5, 6). In this state defibrillation is much more likely to be successful.

The external defibrillator uses an alternating current of 180–720 V, usually 300–400 V (Zol et al., 1956). A current of 5 A is delivered for 0.1–0.2 sec. The electrodes must be at least 7.5 cm in diameter and should be well smeared with electrode paste to ensure good contact. They are applied to the upper and lower ends of the sternum. The machine should have a control which allows the delivery of single shocks or a series of three or six shocks. The leads to the patient should be isolated from the mains by a transformer. There must be two switches to operate the machine so as to prevent inadvertent triggering of the apparatus. The electrodes, if designed to be held by the operator, must be heavily insulated and have an insulating disc on

FIG. 5

Electrocardiogram showing feeble ventricular fibrillation.

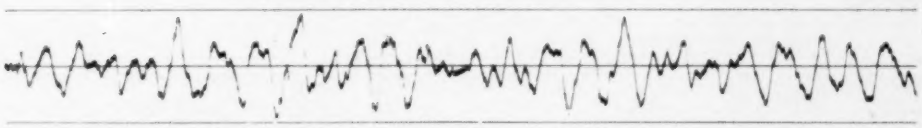

FIG. 6

Same patient as figure 5, showing vigorous rapid ventricular fibrillation after the intracardiac injection of adrenaline.

the handle so that the operator cannot make contact with the metal by accident. An additional refinement is the incorporation of an electrocardiographic oscilloscope monitor on which the electrocardiogram can be recorded at the same time (fig. 7). This must be controlled by a cut-out switch which operates automatically when current is passed through the defibrillator.

A single shock is delivered. If this is ineffective a series of three or six shocks may be tried. Massage must continue between the attempts at defibrillation.

The external defibrillator can be transported a long way to the patient, or the patient may be brought by ambulance to the apparatus while external massage continues. If no external defibrillator is available the patient should be taken to the operating theatre and a thoracotomy performed so that an internal defibrillator can be used.

Restoration of the heart beat after thoracotomy.

The differentiation of cardiac asystole from ventricular fibrillation cannot be made until the pericardium has been opened. Observation through the intact pericardium can be misleading because the fine movements of feeble fibrillation may not be recognized and so the condition may be confused with asystole. Ventricular tachycardia and coarse ventricular fibrillation may be indistinguishable until the pericardium has been opened and the heart inspected directly (Milstein and Brock, 1954). The asystolic heart is relaxed, soft, blue and motionless. The coronary arteries are flattened and their sinuosities straightened out. As a result of hypoxia and the raised venous pressure the coronary veins are black, tense and prominent. Ventricular fibrillation is manifest as a fine or coarse unco-ordinated twitching or writhing of the whole heart muscle. The heart is both pale and cyanotic so that it

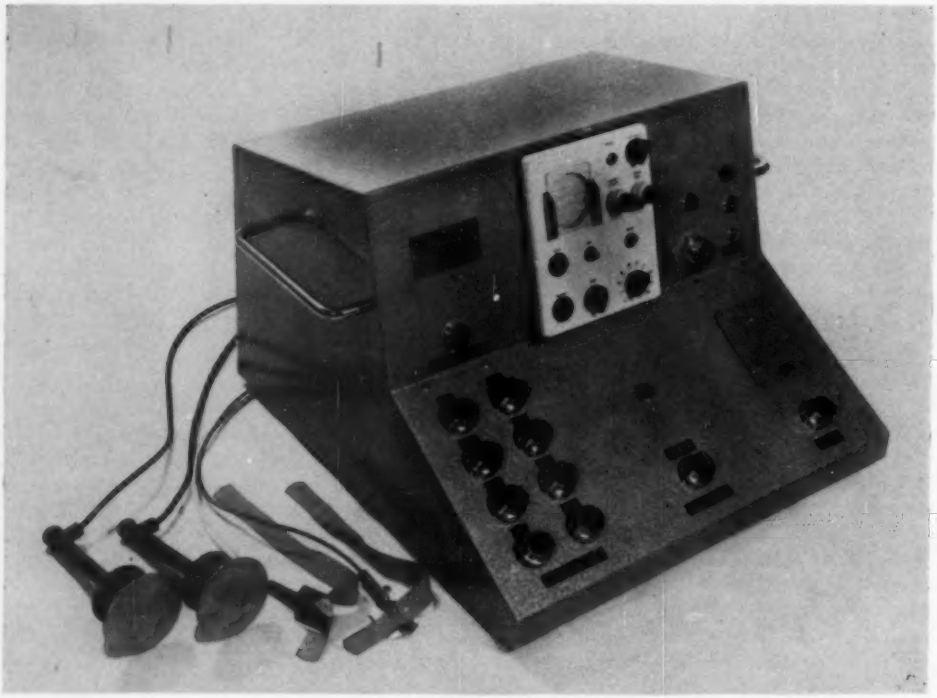

FIG. 7
Combined external defibrillator and electrocardiographic monitoring screen.

has a lavender hue. When ventricular fibrillation is feeble the movement may be so slight that in order to recognize it, it is necessary to peer closely at the heart muscle. The classical sensation of a "bag of worms" is only felt when the fibrillation is vigorous. No movement is appreciated if the fibrillation is feeble. Vigorous fibrillation can also be confused with ventricular tachycardia for on casual palpation it may seem that the contractions are co-ordinated.

The belief that ventricular fibrillation produces a useful, though small, cardiac output is completely false. In terms of cardiac output there is no difference between ventricular fibrillation and cardiac asystole.

When ventricular fibrillation appears it is at first coarse and vigorous, but as the myocardium becomes increasingly hypoxic the fibrillation becomes more feeble and the rate slower over the course of ten to fifteen minutes. Very feeble fibrillation may persist for thirty minutes or more. If the fibrillation responds to treatment the fine movement first becomes coarser and more vigorous and this is accompanied by an increase of tone which gives a sense of resistance when the heart is compressed. Observation of the heart during cardiac massage reveals that the coronary arteries distend and pink lines of oxygenated myocardium appear alongside them. Pink areas then extend out along the branches of the arteries and gradually link up. It is at this stage, which can be promoted by the intracardiac injection of adrenaline, that electric defibrillation is likely to be successful.

The pathological conditions in the two ventricles are not necessarily identical, so that it is not rare to observe one ventricle fibrillating and the other in asystole or beating normally. Such a state of affairs is more likely to be found if one ventricle is hypertrophied or fibrotic as a result of disease.

Treatment of asystole.

If a spontaneous beat does not appear as a result of massage it can be induced by the injection of calcium chloride or adrenaline into the heart. These injections must be made into the cavities of the heart and not into the myocardium. An intramyocardial injection may cause ventricular fibrillation by acting as an ectopic irritable focus. There is no difference in its effect whether it arrives at the coronary arteries in concentrated form or after dilution by passage through the lungs so that it can by injected into any chamber. Although there is a theoretical risk of damaging a coronary artery, or of haemorrhage from the needle puncture, it can be ignored. Those who have little experience in cardiac surgery will find it easier to make injections elsewhere than in the left ventricle for its cavity may be difficult to locate.

Calcium chloride is the drug of choice for the treatment for cardiac asystole for if adrenaline is injected while the myocardium is still anoxic, ventricular fibrillation is likely to follow. The 1 per cent solution is preferable to the commonly used 10 per cent solution. The stronger solution is caustic and may cause severe necrosis if it is injected into the myocardium. A second reason for avoiding the 10 per cent solution is that the volume to be injected is small. The needle may become detached during the injection, and then the dose which has been administered is unknown. A dilute solution of adrenaline is used for the same reason. If treatment is unsuccessful repeated injections of these drugs may be given after further cardiac massage. Under these circumstances overdosage does not seem to be a danger.

Treatment of ventricular fibrillation.

A normal beat can be restored to the fibrillating ventricles by the application of an electric shock. Defibrillation can only be achieved when the fibrillation is rapid and vigorous, a condition which reflects a well-oxygenated myocardium. If the fibrillation is feeble and slow, and the myocardium lacks tone, massage must be continued. If this fails to improve the state of the myocardium, an injection of adrenaline should be given, for this drug usually converts feeble to vigorous fibrillation. Adrenaline injected in the presence of myocardial anoxia can cause ventricular fibrillation. For a long time it was believed that it should not be used in the treatment of fibrillation, but we now know that it is a most effective agent.

The application of an electric shock to the ventricles is designed to render all the fibrillating muscle fibres refractory simultaneously. All muscle contraction then ceases, and after a pause a co-ordinated beat is resumed. Wiggers (1940) advised serial defibrillation with weak repeated shocks

because sometimes a single shock renders only part of the muscle refractory. This method should be used if a single shock fails to defibrillate. A series of three or six shocks is delivered at half-second intervals, but the strength of current should not be reduced.

The defibrillating current is between 1.5 and and 3.8 A. Outside this range the effect of an electric shock is to produce fibrillation (Mackay, Mooslin and Leeds, 1951). The electrical resistance of the human heart is about 100 ohms (Beattie et al., 1953). Voltages of between 100 and 250 are therefore suitable for defibrillation.

Defibrillators must be designed so that they do not damage the heart and cannot electrocute the surgeon. Shephard (1961) discussed the construction of defibrillators and pointed out the dangers of some current commercial models. The simple type in which the two electrodes are connected to the mains with a 1 A fuse on each side of the circuit is particularly dangerous. If the control of current duration is left to an inexperienced operator, a dangerous degree of overheating of the heart may occur. It is therefore an advantage to incorporate an electronic timing switch in the apparatus. There should be a voltage selector giving a choice of potential from 50 to 300 V. The duration of the current should be from 0.1 to 0.2 sec. Burning of the heart may result from the use of an excessive current.

The defibrillator electrodes should be large, so as to cover as much as possible of the surface of the ventricles—at least 7.5 cm in diameter for an adult heart. Their shape is unimportant, but one must be so fashioned that it can be slipped easily beneath the heart. They should be covered with layers of lint or gauze soaked in electrolyte solution in order to make close contact. Saline applied to the heart can cause electrocardiographic changes such as ST segment depression and T wave inversion, and there is a good case for using mammalian Ringer solution instead (Shephard, 1961). The electrode leads, and their junctions with the electrode plates, must be frequently inspected. The leads may break or become detached as a result of corrosion; this renders the apparatus useless. The defibrillator is a vital piece of equipment for the treatment of cardiac arrest and every hospital must be equipped with two of them, for any electrical apparatus is liable to fail.

Method of defibrillation.

While the defibrillator is being assembled and tested cardiac massage is continued. The electrodes are then quickly positioned, one to each side of the ventricles, and held firmly against the myocardium. When the shock is delivered, the patient's limbs may move, and therefore all loose instruments should be removed. The needle of an intravenous infusion may become dislodged, and so the limb into which it is running must be immobilized. If an electrocardiograph is connected to the patient it should be switched off to prevent damage to the instrument.

Defibrillation is attempted with a single shock of 100–200 V for 0.1 sec depending on the size of the heart. If this is ineffective, the duration may first be increased to 0.2 sec and then the voltage stepped up in increments of 50 V. Persistence of the fibrillation calls for serial defibrillation with three or six shocks of 0.1 sec at intervals of 0.5 sec.

During the attempts at defibrillation, the heart must be watched closely. Between each shock or series of shocks, the heart should be massaged so as to maintain oxygenation of the myocardium. If at any time the myocardial tone diminishes or the fibrillation is seen to be feeble, more adrenaline should be injected. Electric shocks must not be given to the toneless myocardium; they will not defibrillate and can only damage the muscle.

When defibrillation is effective, there is a short period of asystole, and then a regular beat returns. If it does not do so, it is probable that too large a current was used. If the asystole persists, the heart must be massaged and the pharmacological treatment for this state applied. One should wait for a time before starting massage because at this stage the heart is in a very vulnerable state, and touching it may cause a recurrence of fibrillation. The electrodes should not be removed roughly or hastily for the same reason.

Sometimes the blood pressure remains low after defibrillation, and the output must be aided by massage. The hands should be removed at intervals so that the heart action can be observed without interference.

Adrenaline occasionally fails to increase tone in ventricular fibrillation. It is then worthwhile to try the effect of an injection of calcium chloride, which may have the same effect. This drug should also

be used to improve the force of contraction after defibrillation if the pressure remains low.

An electric shock is the most effective means of defibrillating the heart, but if the apparatus is not available, defibrillation can sometimes be achieved by an intracardiac injection of 1 or 2 per cent procaine hydrochloride. The dose is 100 mg. If defibrillation does not result, the tone of the myocardium diminishes and the fibrillation becomes feeble. The situation can be restored by an injection of adrenaline, and after further massage another attempt at procaine defibrillation can be made.

Dangers of electric defibrillation.

Burns of the heart. According to Shephard (1961) a burn is likely if 230 V is used with a current duration of more than 0.2 sec. The burn appears at the site of application of the electrodes (fig. 8). The most important factor is the duration of the stimulus. The risk of burning can be diminished by using large electrodes, and by obtaining close application to the ventricles with the aid of gauze padding dipped in an electrolyte solution. The burn may involve the epicardium and part of the thickness of the myocardium in coagulative necrosis, and bubbles may appear in the surface coronary vessels. The best protection against burning is the use of a defibrillator having a fixed stimulus duration.

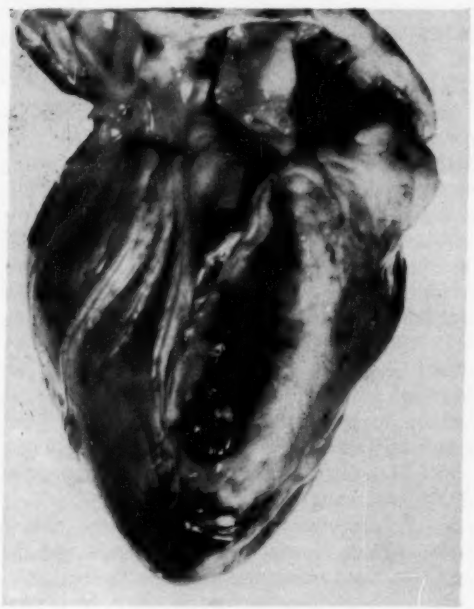

FIG. 8

Myocardial burn caused by excessive duration (0.5 sec) of twelve defibrillating shocks of 110 V.

Electrocution. This is certainly a risk with a defibrillator in which the electrodes are directly connected to the mains. An interposed transformer diminishes it considerably, although with the external defibrillator such large voltages are used that a danger remains. Rubber gloves must be worn by the operator holding the electrodes. If he has massaged the heart his gloves may have become perforated. For protection he should change them or wear a second pair over the first.

Explosion. Any explosive anaesthetic agent in use should have been abandoned at the onset of cardiac arrest, for from that moment the lungs should be ventilated with oxygen only. Before the defibrillator is used, bottles of explosive agents should be removed from the theatre. A further precaution is to avoid placing the electrodes in close proximity when they are not in use, for a spark could result if the circuit is closed accidentally.

Indications for abandonment of resuscitation.

If it is known that an interval of more than ten minutes has elapsed between cardiac arrest and the establishment of an effective artificial circulation the attempt at resuscitation can be abandoned, for though the heart may be restarted fatal cerebral damage will have resulted. During cardiac massage, the pupils should constrict, the carotid pulse should be palpable, and the skin colour should improve. If none of these signs have appeared after massage for half an hour, or if they disappear after returning and remain absent for the same period, it is certain that there is gross irreversible brain damage. Failure to maintain the circulation is then usually due to complete absence of tone in the myocardium because it is no longer viable. So long as tone persists, or the state of the myocardium is changing from fibrillation to asystole and periods of spontaneous beating, there is still a likelihood that the beat will be restored.

Finally the myocardium fails to respond to massage or the injection of drugs, and remains

soft and toneless. Small areas of slow fibrillation may be seen. The blood pressure cannot be maintained. The myocardium has now suffered irreversible changes, and further attempts at resuscitation are useless.

Before this stage has been reached, if no response has been obtained from the heart, the whole of the resuscitation technique must be reviewed to ensure that no important step in treatment has been omitted. This requires attention to the airway, the pulmonary ventilation and the technique of cardiac massage. The cause of the arrest must be considered, and if still acting it must be eliminated if possible. The heart must be inspected for evidence of disease, and especially for a valve obstruction which could be relieved. If the cause of the arrest is a coronary occlusion, there may be no visible signs of it at this stage.

Further treatment after restoration of the heart beat.

When the heart beat has been restored the blood pressure usually rises to a normal level but on some occasions, especially in the presence of heart disease, or after prolonged massage, it may remain low. A systolic pressure of 90 mm Hg is acceptable, but if this is not maintained a vasopressor drug should be given, either by a continuous intravenous drip or by intermittent injections. It may be necessary to continue this treatment for hours or days until the blood pressure has stabilized.

Recurrence of cardiac arrest.

After cardiac arrest has been overcome, a recurrence may occur within a short time. This period is usually only minutes after restoration of the beat but it may be hours later. For this reason the chest is not closed immediately the beat is restored, and a period of thirty minutes is allowed while the heart is kept under observation. When the patient returns to the ward, resuscitation apparatus should accompany him. The heart beat should be monitored with the electrocardiograph for the subsequent 24 hours.

Return of spontaneous respiration.

When cardiac massage is started promptly, respiration may return in a few minutes. If the chest has been opened it may be necessary to anaesthetize the patient at this time and to abolish respiratory movements. When several minutes of delay precede the production of an artificial circulation, respiration generally returns within one or two hours, and the patient can still recover completely, but mechanical ventilation will be required. A delay of 12 hours before the patient breathes spontaneously usually implies a fatal outcome, for the duration of respiratory arrest is a reflection of the degree of anoxia.

If a surgical operation is in progress at the time of the cardiac arrest it is suspended until the heart beat returns. The surgeon must now decide whether to complete the operation. In general, the operation should continue, for the risk of a further episode of cardiac arrest is not great. The condition which necessitated the operation may have caused the cardiac arrest, and may do so again unless the operation is completed. Cardiac operations and operations to deal with haemorrhage fall into this category. If, on the other hand, the operation had not started, and was an elective one, which perhaps would involve prolonged anaesthesia and deterioration in the patient's general condition, it should be abandoned.

Closure of the incision.

As it may not have been possible to obtain the services of a thoracic surgeon any doctor may find himself performing this operation. The steps involved in closing the thoracic incision will therefore be described in detail.

A search for bleeding points must be made. The internal mammary artery at the front of the incision and the intercostal artery at the posterior end must be inspected, and ligated if they have been divided. The pericardium should not be closed completely but a few sutures should be inserted at the lower end of the pericardial incision to prevent the apex of the heart from herniating out of the sac. Complete closure might result in cardiac tamponade from haemopericardium.

A drainage tube is inserted into the pleural space through a small intercostal incision in the ninth or tenth space and fixed in position with a skin suture. The free end of the tube is connected to an underwater drainage bottle. To counteract the risk of infection, 1 g of streptomycin and one million units of penicillin should be

placed in the pleural sac and powdered on to the edges of the incision. For the same reason the incison should be sutured with catgut, for non-absorbable sutures may encourage or perpetuate infection. A few sutures should encircle the ribs adjacent to the incision. The remainder of the incision is sutured in layers so that it is finally airtight.

On the following day an X-ray picture of the chest is obtained. If the air in the pleural space has disappeared the tube is removed.

Postoperative management.

The advice of a thoracic surgeon and a cardiologist should be obtained for the postoperative treatment. The pulse and blood pressure must be recorded frequently for the first 24 hours, and the electrocardiogram must be regularly recorded. A combination of wide-spectrum antibiotic drugs is given for ten days. Infection after an emergency thoracotomy is rare if this precaution is taken. A fluid balance chart is maintained so that urinary suppression from renal anoxia or fluid retention indicative of congestive heart failure can be detected early. The serum electrolytes are estimated daily and careful watch kept for a rise in the serum potassium level, which requires urgent treatment.

Fluids should not be given indiscriminately by vein, for they may precipitate cardiac failure or increase the degree of cerebral oedema. The only indications for their use are persistent hypotension, when pressor amines must be given, and for the treatment of haemorrhage. Hypotension may persist for days, and must be combated by the administration of pressor drugs until the blood pressure stabilizes. Adrenal exhaustion may contribute to this state and hydrocortisone can be of value, but the risk of fluid retention must be remembered.

Cardiac complications.

Many forms of arrhythmia may develop after cardiac massage. The commonest is tachycardia, which usually disappears in five to seven days. The tachycardia, whether it be of sinus origin or due to atrial fibrillation or flutter or a ventricular arrhythmia, may be responsible for hypotension. It is wise to digitalize all patients who have had a period of cardiac massage, for digitalis improves myocardial function as well as slowing the rate.

Right heart failure, as shown by a raised jugular venous pressure, is not infrequent after cardiac massage and should be treated by the usual routine of digitalization and dehydration.

Electrocardiographic changes.

During the treatment of cardiac arrest the electrocardiogram shows unusual transient or permanent changes which are not fully understood. At first changes due to anoxia—bradycardia, S-T segment depression and bundle branch block—predominate. Recovery of the heart beat is often associated with the emergence of a ventricular pacemaker and there may be multiple ventricular ectopic beats which proceed to paroxysmal ventricular tachycardia and ventricular fibrillation. Atrioventricular dissociation is also commonly seen.

After defibrillation of the heart there is gross prolongation of the QRS complex and S-T segment elevation, changes which gradually decrease in magnitude over a period of a few hours, by which time the electrocardiogram may be normal. Some of the changes—bundle branch block, complete heart block, and atrioventricular dissociation—may persist for as long as two weeks and then disappear completely.

The high peaked T wave which is sometimes seen may be due to the administration of potassium salts or to mobilization of endogenous potassium (Le Veen et al., 1960). It has been suggested that most of the abnormalities which persist after restoration of the beat are due to myocardial infarction (Hebert, Iverson and Davidson, 1949; McMillan, Cockett and Styles, 1952), but this seems unlikely, for there is no good reason why the myocardial damage should be localized rather than diffuse. The changes are probably due to generalized myocardial anoxia and to electrolyte disturbances in the myocardial cells.

Pulmonary and air embolism.

These two conditions present special problems in treatment. If sudden cardiac arrest occurs from massive pulmonary embolism, cardiac resuscitation is ineffective unless the obstruction can be removed. Pulmonary ventilation and external cardiac massage must be started immediately. The difficulty is to make the diagnosis, and especially to differentiate the condition from myocardial

infarction. Clinical examination and the electrocardiogram are of no value once cardiac arrest has occurred, and a history of femoral vein thrombosis or of a previous pulmonary embolus may be the only diagnostic features. If the diagnosis is made or suspected, a thoracotomy should be performed and the embolus removed. More often in these patients, cardiac arrest occurs during pulmonary embolectomy, and then the routine for cardiac resuscitation must be started.

Air embolism may cause cardiac arrest in several ways. If air reaches the right side of the heart it may fill the right ventricle, which is then unable to propel blood into the lungs. This may follow the intravenous injection of air or the opening of a large vein during an operation. If treatment is to be successful the operator must realize instantly what has occurred. The chest should be opened and the right ventricle aspirated to remove all the air before starting cardiac massage. Massage before removing the air forces it into the lung vessels causing multiple pulmonary air embolism. This prevents gaseous exchange so that ventilation is ineffective. Cardiac arrest then becomes irreversible.

If air enters the left side of the heart it may give rise to coronary air embolism, which results in immediate ventricular fibrillation. The bubbles of air can be seen in the coronary arteries and subsequently in the coronary sinus. The air can be forced through the coronary system by cardiac massage, which may have to be continued for an hour or more. When this has been done the heart can be defibrillated in the usual way.

Air may enter the cerebral circulation, especially during needling of the chest, by travelling along the extradural venous plexus. The cardiac arrest which results may be reflex or it may follow anoxic convulsions. Treatment for cardiac arrest must be begun immediately; at the same time the patient must be placed in the Trendelenburg position, which allows the bubbles of air to float upwards away from the cerebral vessels.

Anoxic brain damage.

If there has been delay in the treatment of cardiac arrest anoxic brain damage of varying degrees may occur. The amount of damage is influenced by the duration of circulatory arrest, the preceding state of oxygenation and the use of cerebral depressant drugs. There is a good deal of evidence that the brain damage is due to vascular injury which causes an increase in the brain volume and a rise in intracranial pressure (White et al., 1942; Atkinson, 1952). When the intracranial pressure rises, some arteries passing close to fixed structures may be pressed or kinked against them (Lindenberg, 1955). The pathological condition may be further aggravated by intravascular thrombosis (Crowell et al., 1955).

Clinical features. The neurological state resulting from cerebral anoxia due to circulatory arrest may vary between the extremes of a slight delay in return to consciousness and a permanent decerebrate state. A single examination of the patient may yield little information on which to base a prognosis, for this is largely dependent on the duration of the circulatory arrest. A careful history of the timing of the events in the catastrophe is often the best guide to prognosis.

In the most favourable circumstances, consciousness and spontaneous respiration may return before the heart beat recovers. This is exceptional. Usually if treatment has been immediate and effective, respiration returns within twenty minutes and consciousness within an hour or two. There are no neurological complications.

In those patients in whom treatment has been delayed or hypotension has persisted for a time during or after cardiac massage, recovery is delayed. Coma may persist for hours or days. Convulsions or noisy and irrational behaviour are indicative of cerebral oedema, and call for dehydration therapy. An extensor plantar response without other neurological signs has no great significance, but absence of reflexes and spasticity of the limbs indicate a greater degree of cerebral damage. In these patients recovery is possible, but residual neurological damage such as hemiplegia, loss of vision, aphasia, paralyses or sensory loss may persist. There may be serious mental changes ranging from temporary emotional disturbances to a permanent child-like state. Late sequelae include epilepsy and Parkinsonism. Where cerebral anoxia has been prolonged, the patient remains in a decerebrate state with dilated pupils, spasticity of the limbs, and sometimes generalized convulsions. Death does not always supervene in such patients, who may survive for years if their management is pursued with great enthusiasm.

Prognosis. Persistence of coma, status epilepticus or pupillary dilatation for more than a few days are very unfavourable features, although recovery has occurred after coma lasting as long as ten days. Hyperpyrexia also carries a bad prognosis, but this is in part due to the additional damage resulting from the increased cerebral metabolism, and can be countered to some extent if the condition is treated vigorously. Repeated neurological examinations should be made at frequent intervals in the early stages, for the signs may change rapidly and give a definite indication of improvement or deterioration.

Treatment. The routine management for an unconscious patient must be adopted, including if necessary tracheostomy and mechanical ventilation. The treatment is too well known to be discussed in detail here. Convulsions must be controlled by dehydration therapy or generalized hypothermia, for anoxia from this cause adds to the brain damage and may be fatal. It may be necessary to administer a muscle relaxant drug for this purpose. Relaxant drugs are to be preferred to a barbiturate for the control of fits, for cerebral depressant drugs may increase the cerebral damage.

Dehydration therapy. The indications for dehydration treatment are persistent coma, restlessness, noisy or irrational behaviour or persistence of abnormal neurological signs. It should be started immediately. If coma and neurological signs persist in spite of this treatment, hypothermia is necessary. The object of dehydration therapy is to reduce brain volume and perhaps diminish cerebral oedema. For this purpose hypertonic sucrose, concentrated plasma, or hypertonic urea solutions may be used. Sucrose is given by intravenous injection of 50–100 ml of a 50 per cent solution at intervals of three to four hours. There is a risk of renal damage from repeated injections (Lindberg, Wald and Barker, 1939) and extravenous injections may cause severe local reactions. Four times concentrated plasma is administered as a continuous intravenous infusion of 100 ml/hr.

Hypertonic urea has been used successfully for diminishing brain volume after head injuries (Watkins, Stubbs and Lewin, 1961) but not as yet in the case of anoxic brain damage. Nevertheless it would appear to be the most effective dehydrating agent under these circumstances. For the details of its administration the paper by Watkins and his colleagues should be consulted.

If dehydration treatment does not produce an immediate and lasting improvement, hypothermia should be started. Hypothermia benefits the patient in several ways. The cerebral oxygen consumption falls (Rosomoff and Holaday, 1954; Albert and Frazekas, 1956); this provides some protection in anoxic states. The cerebrospinal fluid pressure falls (Rosomoff and Gilbert, 1955), and the brain volume diminishes. It has been calculated that at 25°C there is an increase in the extracerebral space of 55 ml in the average adult (Rosomoff and Gilbert, 1955). Hypothermia also controls the hyperpyrexia that often accompanies brain damage.

Several observers have demonstrated the protection afforded by hypothermia in experimental animals subjected to cerebral anoxia. Williams and Spencer (1958) showed that—after arrest of the cerebral circulation for ten minutes in dogs—hypothermia for 18–36 hours at 32–34°C diminished the mortality from 83 to 25 per cent. Rosomoff and Gilbert (1960) showed that in dogs hypothermia induced soon after cerebral injury prevented permanent brain damage but if it were delayed for seven to eight hours there was no protection. Wolfe (1960) induced ventricular fibrillation in dogs for five minutes, and then lowered the body temperature to 31°C. One-third of the dogs recovered completely, and two-thirds received some protection from cerebral damage.

Williams and Spencer (1958) reported four patients treated by hypothermia at 30–34°C whose hearts had been arrested for five minutes or more. They maintained the hypothermia for 24–72 hours. All survived, three of them without neurological damage.

Hypothermia should be begun if there is persistent coma, or abnormal neurological signs, or as soon as hyperpyrexia is diagnosed. The body temperature should be lowered to 31–33°C by surface cooling. This is simply achieved by allowing electric fans to play on a wet sheet which covers the patient. Shivering is controlled by the intramuscular injection of chlorpromazine. The temperature, blood pressure and the electrocardiogram are recorded at frequent intervals. The blood pressure falls as the temperature is lowered

and it must be maintained by giving vasopressor drugs. Metabolism is depressed in the hypothermic state so that drugs should be given in small doses, for their action is prolonged. If there is difficulty in removing bronchial secretions or any evidence of respiratory depression, tracheostomy and mechanical ventilation should be used without hesitation.

Hypothermia should be maintained for at least 24 hours and should be continued until maximal improvement in the neurological state has occurred.

The probability of intravascular thrombosis contributing to cerebral damage has already been mentioned. Although I have not used heparin in patients with cerebral anoxia its administration would be logical. If it is to be used, 50–100 mg should be given as early as possible after the onset of circulatory arrest to ensure distribution as soon as cardiac massage is started. Further intravenous doses are given at four-hourly intervals. Alternatively it can be given by intravenous drip using a solution containing 100 mg of heparin in 500 ml of glucose-saline infused over a period of six hours. Particular care must be taken over haemostasis if the chest has been opened, and one must be on the alert for signs of intrathoracic bleeding in the postoperative period. It would seem reasonable to maintain heparinization for a period of 48 hours.

Hyperpyrexia must be prevented by taking measures to lower the temperature as soon as it begins to rise. Frequent temperature recording is therefore essential. Hypothermia must be induced immediately and rapidly if damage from hyperpyrexia is to be avoided.

After recovery from coma detailed neurological and psychiatric examinations must be made to assess the residual damage. Prolonged treatment may be necessary to rehabilitate the patient with residual paralysis or spasticity, and psychiatric help is often required to deal with emotional disturbances. Both neurological and psychiatric disorders may continue to improve for many months. A final prognosis should not be given until it is certain that no further improvement can occur.

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BLOOD LOSS AND BLOOD TRANSFUSION

BY

D. LEHANE

Regional Transfusion Centre, Liverpool, England

THE ASSESSMENT OF BLOOD LOSS FOLLOWING INJURY

The assessment of blood loss following injury may be of considerable value when considering the question of replacement of such loss. The clinical picture of "traumatic shock"—hypotension, pallor, coldness of the extremities and cyanosis, suggests that urgent treatment is necessary. However, this picture may not be evident immediately after injury, despite its severity, particularly in young healthy individuals, and its development may be delayed for some hours until the compensatory mechanism begins to fail. It is therefore of the utmost importance to have a means of assessing the probable blood loss so that treatment may be initiated before the clinical picture of "shock" has become obvious. The aim should be to obtain an estimate of the probable loss which, while it will not be exact, will nevertheless provide a reasonable basis for resuscitation.

As a guide to the volume of tissue damage the patient's hand is taken as the unit. The open hand is used as a measure of the damage in superficial wounds and the closed fist to assess the volume of bruised or pulped tissue. In a man of average size the volume of the hand is just under half a litre (Grant and Reeve, 1951). The foot, knee, forearm and upper arm are approximately equal in volume (the foot and knee each rather less and the upper arm rather more than the forearm) and each is roughly equal to 2–3 times the volume of the hand. The leg volume is 4–5 times and the thigh volume 10–12 times that of the hand.

In their report Grant and Reeve (1951) grouped injuries under four categories according to size in terms of the volume of tissue judged to be damaged:

(1) Small wounds—damage less than 1 hand, blood loss seldom more than 20 per cent of the initial blood volume and commonly less than 10 per cent
(2) Moderate wounds—damage of 1 or more hands but less than 3, average loss 30 per cent.
(3) Large wounds—damage of 3 or more hands but less than 5, average loss 40 per cent
(4) Very large wounds—damage of 5 or more hands, average loss 50 per cent

They found these guides reliable in limb injuries but in dealing with abdominal injuries, where they could not be applied, their clinical assessments of blood loss were often at fault. They state that assessment must be correlated with other evidence of blood loss derived from the clinical condition of the patient, and that even if the patient does not seem ill, large and particularly very large wounds almost certainly indicate gross blood loss and the urgent need for transfusion.

Clarke and Fisher (1956) devised a method of assessing the extent of extravasation of blood into the tissues. This consists of cutting strips of felt of known but different volumes and wrapping these about the part of the normal limb to simulate the swelling of the injured limb. This can assist in the recognition of volumes of swelling in the acutely injured patient simply by sight and touch. In addition the method can be applied to the trunk. Clarke and Fisher (1956) maintain that a valuable aid to the estimation of blood loss at all stages consists in training the eyes of clinical observers to appreciate the appearance of known volumes of blood in different situations. They also suggest the use of a polythene bag to envelop the injured limb so that the blood collected in the bag can be measured.

Systolic blood pressure.

Grant and Reeve (1951) found that blood loss was in general associated with a lowered blood

pressure, their findings being that in previously untransfused patients a systolic pressure of 100 mm of mercury or more indicated a blood volume of at least 70 per cent of normal. A systolic of less than 100 mm was indicative of a blood volume of less than 70 per cent of normal.

It is not possible to obtain precise information of the patient's blood volume or haemoglobin concentration prior to injury nor is it possible to measure accurately the amount of blood lost prior to admission; therefore any estimation of the amount lost will not be exact. A reasonably accurate figure may be computed to aid decisions about treatment by taking into consideration the following:

(*a*) The condition of the patient, namely the condition of the skin, whether warm and dry or cold and clammy, the blood pressure, the pulse rate and volume. These must be considered with due regard for the time following injury and also the environmental conditions.

(*b*) Information regarding the amount of blood lost obtained from the patient himself and from observers.

(*c*) Assessment of the amount on clothing, dressings, etc.

(*d*) The extent and location of the injuries.

Assessment of blood loss at operation.

The measurement of blood lost during operation may be done by one of the following methods:

(1) Swab weighing.
(2) Weighing the patient.
(3) Estimation of the haemoglobin content of washings of swabs together with that of blood aspirated from the operation field.
(4) Blood volume estimations.
(5) The electrometric method.

(1) *Swab weighing.* All swabs and towels are weighed prior to use and after use, the gain in weight being taken as the weight of blood on the materials. One gram gain in weight represents approximately one millilitre of blood lost. Used swabs should be weighed without delay as evaporation will lead to error. This method of estimation is simple but has the following disadvantages: (*a*) a considerable error is possible because of the large number of weighings which may be necessary; (*b*) not all blood lost is taken up on the swabs; (*c*) dry swabs and towels must be used throughout; saline packs or towels will invalidate the results. Blood aspirated from the operation site must be collected and measured, and this amount added to the total.

(2) *Weighing the patient.* Using two hospital chair weighing machines, it is possible to estimate the total loss of body weight of the anaesthetized patient in the operating theatre in stable conditions (Rains, 1955). Corrections must be made for the amounts of fluid aspirated or given, tissues removed, dressings and ligatures added, and the loss of fluid by way of the skin and lungs.

(3) *Estimation of haemoglobin content of washings of swabs together with that of blood aspirated from the operation site.* By this method blood loss is estimated by washing bloodstained swabs and towels in a washing machine or tub containing a known quantity of water. The amount of haemoglobin present is proportional to the blood on the swabs and towels. Aspirated blood may be added to the tub or collected and measured separately. The haemoglobin concentration in the tub is estimated by adding either dilute alkali (alkaline haematin) or dilute acid (acid haematin) and estimating the haemoglobin by means either of an ordinary colorimeter or photo-electrically. This method of estimating blood loss requires that the patient's pre-operative haemoglobin concentration be known. It is subject to considerable inaccuracy; for example fat extracted from the swabs will interfere with light transmission, blood contained in excised tissues will not be taken into the result and may be difficult to estimate, changes in alkaline haematin occur on standing, and finally it is difficult to extract completely the haemoglobin from blood clot.

(4) *Blood volume estimations.* The patient's blood volume can be estimated by the use of the dye, Evan's blue (T.1824). A known amount is injected and after allowing time for mixing, the dilution of the dye by the blood gives a measure of the plasma volume. From this the blood volume can be calculated by using the haematocrit reading. This method is not easily applied to estimations of loss during operation. Inaccuracies will occur in the presence of haemolysis or lipaemic

plasma and variations in haematocrit readings, and in addition there is the difficulty of doing two estimations in a short space of time. The use of tracer elements in the estimation of blood loss offers more prospect. Red cells are labelled with 51 Cr and the loss calculated as follows:

$$\text{Blood loss (ml)} = \frac{\text{Fraction of dose on swabs, etc.}}{\text{Fraction of dose per ml of blood}}$$

The blood on swabs, towels etc., is measured as a whole in a ring counter (Veall and Vetter, 1958).

(5) *The electrometric method.* This method depends on the fact that blood is an electrolyte solution which has a constant conductivity value. Therefore, measuring the variations in conductivity resulting from the addition of blood to a liquid of known conductivity will give the blood loss. The necessary apparatus consists of a stainless steel tub fitted with a pulsator (on the principle of a washing machine) together with a measuring device. During operation all blood-stained swabs, dressings and linen are put in the tub so that the blood is washed out by means of the pulsator; blood from the operation field is carried directly to the tub by means of a suction pump. The measuring head (Wheatstone Bridge with an alternating current) estimates variations in conductivity of the liquid; the signals from the head are passed through an amplifier and fed into a servomotor which operates a pointer on a calibrated scale from which the amount of blood lost can be read. Since conductivity is increased with increasing temperature, the machine is fitted with automatic temperature compensation. The use of sodium chloride solution for moistening towels or for irrigation must be avoided. A non-electrolyte substance must be substituted and Le Veen and Rubricius (1958) recommend 2½ per cent glucose solution. The ease and accuracy of measurement with this machine is such that the method surpasses the other methods of blood loss estimation and the instrument is claimed to be accurate to one-half of 1 per cent.

TRANSFUSION REACTIONS

Haemolytic reactions.

Transfusion reactions are divided into haemolytic and non-haemolytic. A haemolytic reaction is defined as the occurrence of an increased rate of destruction of the red cells of either the donor or the recipient as a consequence of transfusion (Mollison, 1956a). Most of these reactions are due to incompatibility between the blood groups of the donor and recipient, and usually it is the donor cells which are haemolyzed. The clinical picture of a haemolytic reaction may also occur as a result of the use of over-age stored blood or of blood which has been haemolyzed by overheating.

The destruction of red cells as a result of transfusion of incompatible blood can occur intravascularly in which case haemoglobin is released into the plasma, or extravascularly in which case the red cells are withdrawn from the circulation without the appearance of haemoglobin in the plasma.

The signs and symbols of incompatibility vary considerably in severity. The usual symptoms are a feeling of coldness, perhaps associated with shivering and possibly rigor, pain in the chest and loins; sometimes the patient complains of hot flushing of the face and there may be a sense of constriction of the chest associated with loin pain.

In an anaesthetized patient, all symptoms are absent and evidence of incompatibility may not be apparent unless the reaction is so severe as to produce a dramatic fall in blood pressure; an occurrence which should suggest the possibility of a transfusion reaction in the anaesthetized patient.

Haemolytic transfusion reactions may result from (1) technical errors in grouping and cross-matching, (2) the use of group O as "universal" donor blood, (3) sensitization of the recipient by previous transfusion or pregnancy to Rhesus or other blood group systems, (4) errors of human fallibility—it is probably true to say that the majority of haemolytic reactions are due to clerical errors. These can only be minimized by the enforcement of a rigorous system of checking to ensure positive identification of the patient. Accidents have been reported in which the laboratory had prepared blood for two patients of the same surname, and because of the failure to supply adequate details of each patient the wrong blood was transfused.

Precautions to prevent haemolytic transfusion

reactions, therefore, are technical and administrative. Technical precautions consist of the adoption of a reliable method of grouping and cross-matching which should be carried out by experienced workers who are thoroughly conversant with the techniques. The use of "rapid techniques" should be avoided except in an extreme urgency. Urgent demands for cross-matched blood for transfusion can often be avoided by good planning.

Safeguarding the patient against clerical and administrative errors is very much more difficult as it is well-nigh impossible to cover all possible eventualities. Therefore it behoves those responsible to ensure that everyone involved in the handling of blood for transfusion adheres strictly to the system of checking laid down. Delegation of responsibility to junior nursing staff should be avoided. The anaesthetist should always check meticulously the patient's particulars on the bottle label with those entered on the case sheet before setting up transfusion.

It is known that a significant proportion of group O bloods contain haemolysins of sufficient potency to cause haemolytic reactions in recipients whose blood groups are other than O. Therefore, except in cases of real urgency when the ABO group of the recipient cannot be determined, group O blood should be used only for group O recipients.

Non-haemolytic reactions.

Circulatory overloading. This is by far the most dangerous of the non-haemolytic reactions and can be caused by surprisingly small amounts of blood in patients suffering from long-standing anaemia or from myocardial insufficiency. If the early signs and symptoms are not recognized and appropriate action taken, collapse and death will rapidly ensue from acute dilatation of the right heart.

This reaction can be avoided by careful assessment of the patient's condition and regulation of the volume and rate of transfusion to the capacity of the patient's heart. The first sign of cardiac embarrassment is failure of the jugular veins to empty. If this sign should be observed transfusion should be temporarily interrupted until emptying of the jugulars is re-established, after which the transfusion may be restarted but only at a very much slower rate. Should the degree of overloading have produced more severe signs, such as those of pulmonary oedema, then more active measures will be urgently necessary.

It is obvious that the immediate need is to reduce the amount of blood in the venous circulation and a useful means of achieving this is by the application of tourniquets to the limbs in such a matter as to prevent venous return but without occluding arterial flow; in this way blood will be dammed back in the extremities and the effect will be similar to a venesection.

Great care is necessary when releasing the tourniquets; this must be done very slowly. This obstruction of venous return for 25 to 30 minutes will be equivalent to a temporary venesection of about 750 ml of blood.

The usual sequence of signs and symptoms in this condition is flushing of the face, engorgement of the jugulars, a sense of constriction of the head, spreading rapidly to the chest, rapid feeble pulse, pulmonary oedema and collapse.

Air embolus. This accident is most likely to occur when positive pressure is applied to the transfusion by pumping air into the bottle. It can also occur without the application of positive pressure if the control clamp is applied high up on the delivery tube close to the bottle, so that if there should be a minute leak in the system the head of blood below the clamp may produce a negative balance whereby minute air bubbles are drawn into the stream and into the circulation; the amount of entrained air may be sufficient to produce a dangerous embolism. Placing the control clamp close to the lower end of the delivery tube will obviate the risk of this occurring and will result, at worst, in a slight leak through any defect higher up.

When positive pressure is applied to a transfusion by pumping air into the container, the risk of air embolus is considerable and it is absolutely essential that the transfusion should be closely watched by an experienced observer, and before vigilance is relaxed the pressure should be released. Air under pressure can pass into the circulation from a bottle which contains a considerable quantity of blood, the level of which may be as much as 2 inches above the outlet. The sequence of events is as follows: partial blocking of the filter results in restriction in the rate of

blood flow through the mesh so that when the blood level falls below the top of the assembly, air passes through and into the vein. For this reason positive pressure should not be maintained once the upper part of the filter assembly becomes visible above the blood.

Allergic reactions. These take the form of urticaria, oedema of the face and bronchospasm, and tend to occur most commonly in patients who are already known to be sensitive to some allergen. The reactions are rarely severe but can be very distressing to the patient. The passive transfer of sensitivity from donor to patient must also be considered (Mollison, 1956b); for this reason it is the normal practice of the National Blood Transfusion Service to reject volunteers who give a history of hypersensitivity. Munoz-Baratta (1955) concludes that allergic and pyrogenic transfusion reactions must be histaminic in type, and that their prophylaxis and treatment is affected by the use of antihistaminic drugs. He claims that good results are obtained by oral administration of antihistamine drugs and that, given parenterally either separately or combined with blood, transfusion reactions of this type are almost completely eliminated. Mollison (1956c), on the other hand, while confirming that antihistamine drugs are effective, considers it unwise to use them as a routine, as it is possible that their action may suppress the characteristic signs of the transfusion of incompatible blood.

Pyrogenic reactions. These result in a rise of temperature to more than 100°F and can best be avoided by scrupulous care in the cleaning of the transfusion equipment and in the preparation of the anticoagulant agent. Distilled water must be freshly prepared and the solutions autoclaved as soon as possible after preparation. All apparatus, glass, rubber tubing and needles must be thoroughly cleaned and receive a final rinse of distilled water, followed by drying, assembly and autoclaving.

A slow rate of transfusion, where possible, will reduce the risk of pyrogenic reactions. In addition it is well known that the severity of pyrogenic reactions can be reduced by keeping the patient warm, even a little warmer than comfortable.

Antihistamine drugs are of value in patients who have suffered this type of reaction from previous transfusions and the administration of such drugs before transfusion will at least mitigate the reactions and will in many instances completely prevent their occurrence.

Safeguarding of the patient against transfusion accidents and reaction depends on the exercise of meticulous care in the preparation of apparatus, the collection and subsequent storage and handling of the blood, strict attention to detail in collecting and identification of specimens, a reliable cross-matching technique, adequate checking to ensure that the correct blood is given, and continuous supervision throughout the duration of the transfusion by experienced personnel.

BLOOD SUBSTITUTES

Plasma. The best substitute for whole blood is plasma, since it will restore and maintain the blood volume in the same way as transfusion of whole blood. Ideally in the treatment of severe blood loss where considerable quantities of fluid are needed, blood should also be given in the proportion of one bottle of blood to two, or at most three, of plasma in order to prevent dangerous haemodilution. Otherwise the properties of plasma are such that it will restore lost volumes and sustain the increase as well as whole blood by virtue of its similar protein content and osmotic pressure. In view of its properties it would be thought that plasma would be used more extensively than is at present the case, the reluctance to use it, in preference to plasma substitutes, to augment blood, stems from the mistaken impression that the risk of transmitting homologous serum jaundice is very much greater with plasma than it is with whole blood. This impression dates from the war and immediate post-war years when the plasma available was derived from the bloods of at least 300 donors; this was known as large pool plasma, and its use resulted in a jaundice incidence of up to 12 per cent (Lehane et al., 1949). However, the plasma now available is derived from the bloods of not more than ten donors, small pool plasma, and it has been found that the incidence of jaundice following its use is not significantly different from that which occurs when whole blood alone is used. In two surveys the incidence of jaundice was as follows: whole blood 0.8 per cent, small pool plasma 1.2 per cent (Lehane et al., 1949); whole blood 0.16 per cent, small pool plasma with or without blood

0.12 per cent (Medical Research Council, 1954). Therefore it would seem reasonable to state that small pool plasma might well be safer than inadequately matched blood, and that where the immediately available supplies of blood were insufficient for an emergency, plasma is the ideal substitute.

Dextran. This is a synthetic substance, the molecules of which are long chains of glucose units; the British product has an average molecular weight of about 200,000. It is a safe and satisfactory substitute for plasma, and although large amounts are said to prolong bleeding time, there is no evidence that moderate amounts have this effect. Bull et al. (1949) found that the plasma protein level was reduced after infusion of dextran and rose slowly again as the dextran was eliminated, thus the total of protein plus dextran tended to remain constant. Although dextran is incorporated in the tissues there is no evidence that it causes histological changes. As reactions to dextran are very uncommon, it may be said to be a safe substitute for plasma which will give good results.

Plasmasan (*Polyvinypyrrolidone*). This substance has been used extensively on the Continent for several years but it appears to be less well retained in the circulation than dextran. It is therefore a less satisfactory plasma substitute.

TRANSFUSION APPARATUS

The present standard glass-rubber transfusion administration set fitted with either a wire gauze or gas-mantle type internal filter is now being replaced by a plastic disposable set with an external nylon filter. This new set also differs from the glass-rubber set in that it has a combined air inlet and blood outlet needle which is pushed through the rubber diaphragm of the bottle, whereas in the glass-rubber set there is a rubber bung carrying both a blood outlet and an air inlet of glass tubing.

Experience with the new plastic sets, which are at present manufactured only by Messrs. Capon Heaton, of Birmingham, indicates that they are very satisfactory and are in general preferred to the older set.

There are many varieties of plastic set of Continental or American manufacture, some of which have what appear to be inadequate filters. Of the American sets the "Plexitron" No. R48, marketed by Baxters, which combines a pressure pump as shown in figure 1, is now obtainable in this country. The pump in this set is part of the combined drip counter-filter chamber and consists of a plastic ball which floats up and closes the inlet when a pumping action is applied to the flexible chamber thereby filling it with blood. In a limited trial this set worked very satisfactorily and it has the merit that there is no risk of producing air embolus when positive pressure is applied.

The Fenwal plastic set is an all-plastic unit including the blood container; this type of unit is also available and is supplied ready charged with the necessary anticoagulant agent and is fitted with a blood collecting attachment. The administration set is a separate unit which when required must be attached to the container by puncturing a diaphragm in a special port in the bag. These units have the merit that there is no air in the

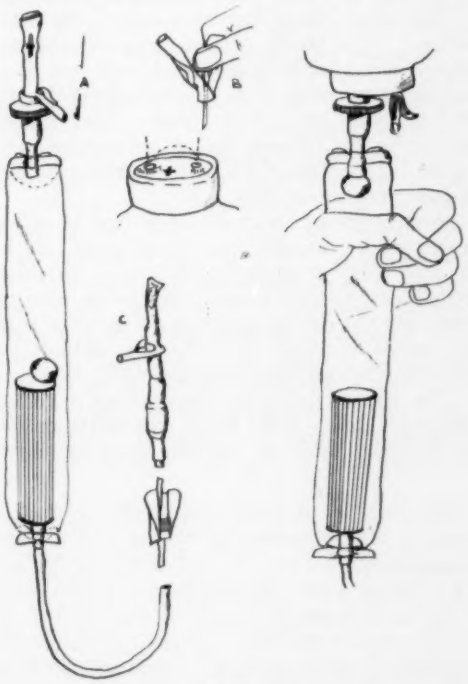

FIG. 1
The Plexitron No. R48 (Baxter's)

container and there is no need for venting as the bag is flexible. Positive pressure can be applied simply by compressing the bag between two flat surfaces or by placing the bag under the patient's buttock. This type of set is not suitable for use at blood-collecting sessions where large numbers of donors are dealt with, because it is necessary after venepuncture to displace a bead valve fitted in the tubing before the blood can enter the bag. This manoeuvre sometimes presents considerable difficulty thus necessitating the spending of more time with each donor than is practicable.

METHODS OF APPLYING POSITIVE PRESSURE

Positive pressure. This may be necessary when the restoration of lost volume is a matter of urgency demanding a rapid rate of transfusion. With massive haemorrhage there will be very marked venespasm and it is advisable if possible to avoid attempts at transfusion through the veins of the leg, as it can present extreme difficulty and indeed it may be impossible to overcome the venespasm.

The most convenient and readily available method of applying positive pressure without special apparatus is to apply the bulb unit of a sphygmomanometer to the air inlet tube of the set and to pump air into the bottle. This method is effective but as mentioned earlier requires very careful supervision if the risk of producing air embolus is to be avoided.

Positive pressure may also be applied by using a roller type pump like the Martin's pump, which is used fairly extensively. This pump provides satisfactory positive pressure, but is not entirely free from the risk of producing air embolus as it is possible to entrain air if the level of blood in the drip chamber falls below the outlet.

The application of positive pressure to transfusion by means of the Baxter administration set or by compression of a plastic blood container, as for example the Fenwal Pack, is free from the risk of air embolus; nevertheless it is imperative that the patient should be watched closely for signs of cardiac embarrassment by an experienced observer throughout the procedure.

When air is used to produce positive pressure the necessity for vigilance cannot be overstressed and the responsibility for maintaining supervision should never be delegated to junior medical or to nursing staff.

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FAILURE OF THE CIRCULATION

BY

JOHN BEARD

Postgraduate Medical School and Institute of Cardiology, London

INTRODUCTION

THE anaesthetist is increasingly extending his responsibilities in both pre- and postoperative care. What is done as a result of the assessment of pre-existing circulatory disorders affects the whole course of anaesthesia including the recovery period; it must be based on a sound knowledge and the application of basic principles common to anaesthesia and medicine. While this section could justifiably contain a major part of the physiology of the circulation as well as of cardiology, it can only be regarded as a classification with appended notes and not as a comprehensive text. An attempt has been made to arrange the subject in such a way as to stimulate thought and further reading from the selected bibliography.

GENERALIZED CIRCULATORY FAILURE

An efficient cardiovascular system requires an adequate pump to discharge into a vascular system whose tone is able to distribute the blood in varying amounts to the different parts of the body and to return it to the pump for recirculation. Inability of the cardiovascular system to supply the body as a whole with sufficient blood for its needs is termed "general circulatory failure". When this occurs the heart does not propel sufficient blood into the arterial tree. If this failure is due to insufficient return of blood to the heart the condition is "peripheral circulatory failure" and includes the results of hypovolaemia. If the heart is being supplied with ample blood then the failure is cardiac. This cardiac failure may, however, only be relative to the excessive demands of a vascular system which may offer an inadequate resistance for the maintenance of a proper filling pressure. Cardiac and peripheral failure frequently occur in combination, the one being consequent upon the other. For example, peripheral failure may be associated with such lowering of peripheral resistance that no heart, however robust, could increase its output to maintain sufficient aortic pressure. In these circumstances, the poor filling pressure and hence the flow in the coronary arteries impairs myocardial function and contributes a "cardiac" element to the vicious circle which is a likely result of a concomitant reduced venous return.

A poor blood supply will have widespread effects which are most obvious in the more vital structures. Elsewhere the effects of deprivation might only later become evident, revealing a deterioration hitherto unsuspected. Protective reflexes and mechanisms are liable to fail suddenly with continued stress, including anaesthesia and surgery—the heart becoming decompensated and hypotension irreversible. Poor perfusion of the tissues leads to incomplete metabolism, whereby lactic, pyruvic and other acids are formed. The kidneys may be unable either to compensate for, or excrete, these metabolites and, if respiratory function is depressed, a respiratory element will be added to the acidosis which itself may cause hypotension with poor coronary filling and a reduction in cardiac output. Liver and renal tubular damage, adrenocortical failure and septicaemia from mesenteric stasis may all contribute to the often terminal picture of circulatory failure.

Since the demands of the body on the cardiovascular system vary, no specific cardiac output can be pronounced to be either adequate or inadequate without consideration of other factors. An increased output is needed to maintain an adequate perfusion pressure whenever the peripheral resistance is reduced. This may be due to marked peripheral vasodilatation or to a shunt from the arterial to the venous system. An increased

metabolism and a lower peripheral resistance occur with fever and thyrotoxicosis. Pregnancy makes extra demands and is associated with an increased blood volume. In these conditions the circulatory system may prove inadequate and failure occurs when the cardiac output is considerably above the resting normal of 3 l./sq. m/min. This level is increased by digestion or exercise, and circulatory failure, particularly in heart diseases, commonly occurs in the first place when the cardiac output, while well above the resting normal, is, however, inadequate for the body's need *at the particular moment* and below that which a normal heart would have achieved in the circumstances. Later, as the condition progresses, failure occurs at rest.

While failure of the heart to pump out enough blood to fill the vascular tree at an adequate perfusion pressure is a basic cause of circulatory failure, this may be in no way the fault of the heart if the venous return is inadequate as in the peripheral failure of extreme hypovolaemia. Even the strongest heart may fail to expel enough blood to maintain pressure in a vascular system with a virtually negligible resistance, but a failing heart with a low output, even if the vascular tree is normally filled and contracted, may eventually produce the same picture of general circulatory failure. Between these extremes is a state in which a heart—adequate for a quiet life—is unable to meet extraordinary demands which would not have taxed a healthy patient.

In summary: generalized circulatory failure may have a peripheral vascular and a cardiac component. During surgical operations the peripheral is often the primary factor while in medicine the cardiac element may be predominant. The lists of conditions from which circulatory failure may develop (see tables I–III) includes so much that detailed discussion is impracticable; they indicate those states which should be kept in mind both in pre-operative assessment and in the handling of patients. They may also serve to give warning in time for prophylactic treatment. Even without this awareness, skilled anaesthetic care of the patient will go far towards a successful outcome.

Generalized circulatory failure due either to peripheral or central causes may be met by the anaesthetist either as a sudden emergency in a previously healthy individual or as a development in a patient already suffering from circulatory embarrassment, in which case a much lesser stress will be enough to destroy the balance hitherto maintained. The recognition of compensated circulatory disorders and an understanding of the mechanisms involved are therefore important.

The features of acute circulatory failure are well known but subject to variation according to the cause. Combinations of consciousness and apathy or an alert restlessness may be noted, together with complaints of thirst and air hunger. The skin when vasoconstricted, is pale and cool, and often sweaty with slight distal cyanosis. The pulse rate is usually fast (unless a vasovagal element predominates—in which case it is slowed). The reduced systolic and pulse pressure makes the pulse feel "thready". The heart sounds are feeble. There is a reduced cardiac output from whose slow flow an increased removal of oxygen leads to an increase in A—V oxygen difference.

Circulatory failure may occur suddenly in acute myocardial infarction. Most often, however, it develops as a breakdown of compensation of some pre-existing state. Hypovolaemia is perhaps the commonest of these in anaesthetic work and the suddenness with which circulatory failure may ensue can surprise even the wary. When due to bleeding, the first sign of the contracted blood volume is vasoconstriction; the skin is pale and cold, and the veins are collapsed. When the vascular tree does not constrict sufficiently to compensate the pulse rate rises and the pressure falls. In some patients the pulse may slow and the pressure falls at an early stage as part of a vasovagal syndrome. This is, however, more common in the experimental subject—especially in response to the anxiety of needle puncture—than in normal clinical practice. Here the blood pressure is usually well maintained or even raised in the early stages as a result of vasoconstriction. This "compensation" may fail to occur under some circumstances which include a vasovagal syndrome as well as adrenocortical deficiency and heat exhaustion. If the normal adrenaline and noradrenaline action is prevented by such drugs as chlorpromazine, reserpine or the ganglion blocking agents, vasoconstriction may not take place. Similarly, in the high output states and in congestive heart failure with its increased blood volume, the veins may

be well filled and here failure may occur in the absence of vasoconstriction.

In hypovolaemia due to bleeding, the earliest change is the transient retention within the blood stream of non-protein fluid which has not passed into the tissues owing to the reduced capillary perfusion pressure. Soon proteins enter the circulation and the plasma volume is increased, occasionally exceeding the volume of red cells and plasma lost. This is maximal at about 72 hours after bleeding and at this stage the haemoglobin and haematocrit readings are reduced. Before this dilution there is no fall in haemoglobin level and while there may be pallor due to vasoconstriction, the waxy paleness of haemorrhage is not seen. Instead there may be peripheral cyanosis; this depends on a sufficiency of unoxygenated haemoglobin, being marked in hypovolaemia—due to fluid depletion—not involving a loss of red cells; it may indicate the possibility of an increased viscosity of the blood which further impairs the capillary circulation. Sludging of the corpuscles may add to the stasis, anoxia and metabolic acidosis. Increased capillary permeability is more likely to be the result of these and is no longer thought responsible for the very large deficits in circulating blood volume. These are, however, late phenomena and are overshadowed in importance by the renal vasoconstriction which may develop a few hours after the bleeding has apparently been well compensated by vasoconstriction and in the absence of hypotension. The stimulus to the renal vasoconstriction appears to be the hypovolaemia rather than hypotension, and the delay in onset is characteristic and may allow time to prevent renal cortical necrosis by prompt transfusion. Once initiated, even when the blood volume has been restored, the constriction is slow to pass off and may be increased by the reduction of renal flow usual with anaesthesia. Haemolysis due to incompatible transfusion and electrolyte disturbance may all accentuate renal damage. If the reduced blood volume occurs in the course of abortion, eclampsia or concealed accidental haemorrhage, the danger of renal ischaemia is much increased.

Damage to the healthy liver is not so prominent after haemorrhage and acute hypovolaemia—the hepatic flow being reduced less drastically pari passu with the reduction in cardiac output. Haemorrhage can precipitate acute liver failure in portal hypertension, and even in the absence of liver diseases patients being treated with anticoagulent drugs of the dicoumarol type, may have a much prolonged prothrombin time after hypotensive episodes. Very severe and prolonged hypotension in dogs has been shown to be followed by the release of ferritin (V.D.M.) from the liver but this has not yet been demonstrated in man. The reduction in splanchnic blood flow, in large measure compensated by increased extraction of oxygen and hence greater desaturation of the portal blood, suggests vasoconstriction. It has been strongly contended that as a result there is an invasion of the blood stream by toxins derived from the ordinary gut organisms, and that these toxins are responsible for much of the shock syndrome. Whether this is so or not there is certainly a high degree of protection by broad spectrum antibiotic drugs in experimental animals subjected to injury, and many are convinced that the toxins of such organisms as B. Welchii are associated with an undue incidence of circulatory failure.

Apart from the reduced blood volume of haemorrhage, trauma and burns, there is an important reduction resulting from losses into, and impaired absorption from, the gut. In these, electrolyte losses may play a significant part in the circulatory disturbance. For example, in ileus the hypokalaemia in addition to tending to perpetuate the ileus and causing lethargy and muscle weakness, may be the cause of cardiac arrhythmias and hypotension with a collapsing pulse. Electrolyte changes are also of importance in other shock-like states. In diabetic coma hyperkalaemia is usual, but if vomiting and starvation have been prolonged and especially if the dehydration has been a little over-treated with potassium-free saline solutions, hypokalaemia may occur.

CENTRAL CIRCULATORY FAILURE

When exposed to stress a heart with previously well-compensated disease may be unable to meet demands and fails. In these circumstances the diminished cardiac output (relative to need) may so reduce the blood flow as to justify the term "forward failure". In the case of the kidney, the normal flow of about 1500 ml/min may

TABLE I

Conditions which predispose to peripheral circulatory failure.

Hypovolaemia		
	Acute	Haemorrhage or plasma loss } Burns, crush injuries.
		Vomiting, obstruction, ileus, diarrhoea, or peritonitis (hypokalaemia), or hyponatraemia.
		Dehydration or diabetic coma. Addisionian crises.
	Chronic	Anaemia.
		Malnutrition, especially in the aged.
		Cachexia.
Toxaemias and infections. (Especially B. Welchii.)		
Metabolic acidosis. Sudden falls in Pco_2.		
Adreno-cortical deficiency. Pituitary dysfunction cachexia.		
Adrenolytic drugs.		
Anaesthetic agents.		
Spinal anaesthesia. Ganglionic blockade. Spinal paralyses.		
Posture.		
Vaso-vagal attacks.		
Cardiac failure.		
I.P.P.R.		

TABLE II

Conditions in which there may be a low fixed cardiac output.

1. *Restriction of cardiac filling.* Constrictive pericarditis. Tamponade. Effusions. Haemorrhage.
2. *Obstructed blood flow through the heart.* Severe valvular stenoses.
3. *Severe pulmonary artery hypertension.*
   - (*a*) *Severe* mitral stenosis with *very high* pulmonary vascular resistance.
   - (*b*) Late stages of "emphysema heart disease".
     (Where the capacity of the pulmonary vascular bed is *severely* restricted)
   - (*c*) Thrombo-embolic obstruction.
   - (*d*) Congenital heart disease. Eisenmenger syndrome.
   - (*e*) Idiopathic.

TABLE III

Conditions with an impaired cardiac action.

1. *Reduced venous return.* Hypovolaemia. Peripheral circulatory failure. } See table I.
   I.P.P.R.
   Mediastinal venous obstruction.
2. *Valvular incompetence.* Tricuspid or mitral obstruction.
3. *Pulmonary artery constriction.*
4. *Failure in high output states.*
   - Fever or pregnancy.
   - Thyrotoxicosis. Beri-beri.
   - Anaemia. Cor pulmonale (CO_2 retention).
   - A.V. shunts. Paget's disease.
5. *Failure due to "internal" shunts.* A.S.D. V.S.D. Patent ductus.
6. *Failure due to bizarre congenital abnormalities.*
7. *Failure due to abnormal rates and rhythms.*
   - Tachycardia or bradycardia.
   - Ectopic beats. Auricular fibrillation.
   - Heart block. Ventricular fibrillation.
8. *Failure due to myocardial insufficiency.*
   - Secondary to fatigue of myocardium.
     - (*a*) Hypertension. Coarctation.
     - (*b*) Valve lesions.
   - Myocardial ischaemia and infarction.
   - Myocarditis.
     - Rheumatic.
     - Diphtheritic.
     - Obscure.
   - Infections. Toxaemias.
   - Anaemia and anoxia.
   - Obesity.
   - Cardiac incisions and wounds.
9. *Citrate intoxication.*
10. *Hypo- and hyperkalaemia.*
11. *Metabolic acidosis.*

be reduced to 500 ml/min. This reduction is due to arteriolar constriction and is not the consequence of "forward failure", in that it is disproportionately greater than the reduction of the cardiac output and, indeed, may occur with high output failure. The glomerular filtration rate then falls and an associated water and salt retention ensues. The hepatic flow, normally 1,500 ml/min is reduced only in proportion to the fall in cardiac output. The cerebral blood flow, on the other hand, usually remains at the normal 800 ml/min. This is surprising in view of the fatigue, undue drowsiness by day and often disorientation and restlessness at night. This mental impairment is probably due rather to renal and hepatic disturbance than to cerebral hypoxia. The failing heart is not helped by the poor filling pressure in the coronary arteries and myocardial distress may be indicated by gallop rhythms and pulsus alternans.

If the vascular system is normally filled and an adequate amount of blood returns to a failing heart, the pressure is liable to rise behind a failing ventricle or ventricles. In left ventricle failure "backward failure" results in pulmonary venous congestion. When the right ventricle fails there will be distended veins especially in the neck and a congested liver. The rise in venous pressure may occur earlier if the blood volume is increased and may follow rapid transfusion in a precariously compensated heart. In congestive heart failure the distended neck veins and engorged liver are due not only to the rather unimpressive "backward" failure of the right side of the heart, but are also the result of the increased blood volume consequent upon the water and salt retention of reduced renal glomerular filtration; the purely renal factor being accentuated in the case of salt retention by an ill-understood element of adrenocortical malfunction with excess activity of aldosterone. The moderately raised pressure in the great veins assists atrial filling and, by increasing the end diastolic muscle fibre length, excites a more forceful myocardial contraction. Should this filling pressure increase beyond the point on the well-known Starling curve at which maximal response occurs, then myocardial efficiency (and hence stroke volume) will decrease. A congestive cardiac failure is commonly the result of hypertensive heart disease, myocardial ischaemia, valvular heart disease or cor pulmonale. At first compensation tends to conceal abnormal signs and symptoms. Later these become manifest when the diminished cardiac reserve is inadequate for the activities of the day. At this stage the heart can still maintain an output above the resting normal but it is not enough and, as a result of reduced kidney filtration, fluid will accumulate progressively. At night, during rest, the output is adequate and the kidney flow increases, the excess fluid being excreted (at the expense of a disturbed night). Later, as the output falls still further it is inadequate even at rest, and back pressure increases in the systemic and pulmonary circulation, decompensation being often hastened by the onset of auricular fibrillation. The terms right- or left-sided failure apply when the strain affects predominantly either the right or left ventricles. Left ventricular failure commonly results from hypertension, myocardial ischaemia or aortic valve lesions. Here the output falls and "backward" failure results in congestion in the pulmonary circuit. A somewhat similar state occurs in mitral valve disease, particularly stenosis. The pressure in the left auricle, pulmonary veins and pulmonary capillaries will be increased and may eventually exceed the plasma colloid pressure; pulmonary oedema is then an ever present risk. Dyspnoea is due to the pulmonary congestion behind the failing heart. This congestion, with its risk of pulmonary oedema, may be held in check by the reduction in output of the right side of the heart as a result of (1) increased resistance to right ventricular output by the raised pulmonary artery pressure, and (2) the reduced right heart filling owing to blood being held up in the lungs and by the reduced size of the right ventricular cavity as a result of the bulging left ventricle. Orthopnoea of left-sided failure may in large part be explained by the different increase in filling pressure of the two sides—a result of recumbency. On the right side, the venous drainage is from the whole body, the greater part of which is below the heart. The horizontal position, therefore, increases the venous return to the right heart. In contradistinction, since the left heart is in the midpoint of its drainage system, the lungs and left atrial filling are not affected to the same extent. As a result, a change from the vertical to horizontal position tends to increase the output of the right more than the left ventricle and thus to lead to overfilling of the

pulmonary circuit; this makes breathing more laboured.

In left ventricular failure, pulmonary oedema implies serious left myocardial damage but in mitral stenotic obstruction pulmonary oedema usually occurs at an early stage in the history of the complaint. A *moderate* narrowing of the valve leads to *moderately* raised left atrial pressure which may, however, be temporarily raised by the increased blood flow of exercise, of pregnancy or of fever. The time available for the blood to pass into the ventricle, the diastolic filling time, may be shortened by the tachycardia due to exertion, apprehension or perhaps atropine. A healthy right ventricle can then raise the pulmonary capillary pressure to well above the critical 30 mm of Hg and oedema may occur. Later in the disease process the continued rise in the left auricular pressure is accompanied by a narrowing of the pulmonary arteries which, while protecting the pulmonary capillaries leads to pulmonary hypertension and eventual right-sided failure; this is in accord with the common experience of the majority of patients with mitral stenosis who are only liable to pulmonary oedema for a short period (if at all) and far more commonly are subject to congestive heart failure several years later. Pulmonary hypertension may also complicate ventricular or, less commonly and at a later stage, atrial septal defect and patent ductus arteriosus. The pulmonary hypertension arises from arterial constriction in response to the torrential blood flow through the pulmonary circuits, which not uncommonly exceeds three times that of the systemic flow of these patients. Should the pulmonary arteries not constrict and reduce this flow, heart failure may result and, in those with a ventricular septal defect, often causes death in the first year of life. The arterial constriction reduces the excessive flow through the lung but may, in doing so, lead to reversal of the shunt and cyanosis. This is the "Eisenmenger reaction" or syndrome. The Eisenmenger *complex* proper is pulmonary hypertension with reversed shunt at *ventricular* level. The reaction is another example of a protective mechanism which may temporarily prolong life. In this case heart failure may have been postponed but at the expense of any chance of surgical correction.

While severe pulmonary artery constriction is a cause of low fixed output, that occurring during the exacerbations of bronchitis in emphysematous patients with cor pulmonale usually develops while the cardiac output is still in excess of normal levels.

The effect of changes in rate and rhythm on cardiac output can be marked. If the heart is completely normal, increasing the rate increases the output within certain limits; thus polyuria is often marked in paroxysmal tachycardia in those with normal hearts. If there is any valvular obstruction as in mitral stenosis, or in myocardial disease, pulmonary oedema or congestive heart failure may ensue. Similarly, coronary narrowing may lead to anginal pain. At very rapid rates, even the normal heart will fail, and syncope on effort is common with extreme tachycardia, the shortened diastole allowing insufficient time for the blood flow, both into the heart from the great veins and also along the coronary arteries to supply the myocardium. While tachycardia may precipitate failure in some patients it may, on the other hand, be essential for survival in constrictive pericarditis and tamponade. Here the venous pressure is already maximal in both systemic and pulmonary veins and little increase in stroke volume is possible. Only by means of a rapid rate can the cardiac output be maintained. By this means—helped by a reflex peripheral vasoconstriction—the aortic pressure can be kept up. Once this falls the coronary circulation, already in difficulties owing to the pressure on the surface of the heart, deteriorates and myocardial failure occurs. Thiopentone induction has a sinister reputation in this context; any agent or technique which combines bradycardia with hypotension would seem even more dangerous.

Bradycardia may be compensated by an increase of diastolic volume and increased stroke volume. Clinically, a raised systolic pressure with a wide pulse pressure results and cannon waves may be seen in the neck veins. Very slow rates, however, lead to congestive failure, and ventricular asystole of more than 10 sec, often causes convulsions. During anaesthesia for cardiac surgery—when intravascular pressures are being recorded—the effects of both fast and slow rates on arterial and venous pressures may be seen.

In general the treatment of tachycardia is directed at the cause, but particularly during cardiac sur-

gery when the patient has not already been digitalized, intravenous digoxin or even neostigmine may be needed to maintain the output. Tachycardia of ventricular origin is, however, often best managed by electrical "defibrillation".

Bradycardia is first treated by small doses of atropine given intravenously. If unresponsive or due to heart block, isoprenaline given intravenously or by rectal suppository is invaluable. Heart block persisting after surgery near the conductive tissue usually needs an artificial pacemaker for at least a few days.

GENERAL CONCLUSIONS

In brief, the effects of general anaesthesia include an increased flow of blood through the superficial tissues with restriction of the splanchnic and especially the renal flow. In the lighter planes of anaesthesia, particularly with ether, there is sympathetic activity which is increased by surgical stimulation. The net result is maintenance of total vascular resistance and systemic pressure. As the depth of anaesthesia increases the cardiac output usually lessens. Probably because it can only be used to provide a superficial plane of anaesthesia, the net fall in peripheral resistance is said to be less with nitrous oxide and oxygen anaesthesia than with barbiturates or more potent inhalation agents. The pallor of nitrous oxide and oxygen anaesthesia is some evidence of a maintained vasoconstriction which demands a lesser increase of cardiac output to maintain systemic pressure. Spinal anaesthesia, ganglion blocking agents, antiadrenaline drugs such as chlorpromazine and higher concentrations of anaesthetic agents all reduce vasoconstriction, altering the redistributions usually seen in general anaesthesia and increasing the effects of posture.

This over-simplified account of the haemodynamics of anaesthesia presents an unduly gloomy picture since it leaves out an important factor which should go some way to mitigate these untoward effects—the anaesthetist. At no time is a patient with impaired circulation likely to have such undivided physiologically and pharmacologically skilled care. This care should be afforded not only during the period of surgery but should extend to the pre- and postoperative phases. Before surgery, the cardiovascular system should be made as near normal as possible. The history and signs of the various conditions listed (see tables I, II, III) will be sought out and, where possible, steps taken for their correction. Fortunately, gastric suction, and intravenous therapy with antibiotic drugs often make some delay possible and helpful before even emergency surgery. The time gained is invaluable if only to enable the body—by renal action and by shifts between the various compartments of the body water—to correct therapeutic miscalculations of fluid and electrolyte need! Blood pressure, volume and haemoglobin levels made normal for even 24 hours will improve tissue oxidation and reduce metabolic acidosis. Reduction of secretions by posture, possibly by bronchoscopy or even tracheostomy and certainly by physiotherapy, together with antibiotic therapy, may improve ventilation. Cardiac rate and action may be helped by digitalis and it is better to give this orally over a day or two according to the accepted rule rather than intravenously on the operating table. On the other hand oedema, hydraemia, and salt retention are better treated by injection: intramuscular mersalyl is faster and more effective than oral treatment by the chlorothiazide group of drugs and is safer because it does not produce such an exaggerated loss of potassium.

Turning in more detail to the assessment of the circulation, the arterial pressure must be considered in conjunction with the pulse rate and the state of the peripheral vessels including the degree of venous filling. The character of the pulse is a well-known guide to the state of the larger arteries. Further information can be gained from sphygmomanometry which can indicate the systolic and pulse pressures. The latter may be so increased when the vascular bed is dilated in high output states as almost to justify the description of "collapsing". The movement of an aneroid needle and, still more, that of an oscillometer can be a useful guide to the degree of vascular dilatation, the latter seeming to give some indication of the total vascular bed and to show any diminution of this before it is demonstrable in the larger arteries. An oscillometer can also be useful when restricted access to the patient makes inspection of the skin difficult. The briskness of the circulation in the skin may be judged by estimating the capillary refilling time after digital pressure. In the normothermic patient

when the skin vasoconstricts, the tissue will, if exposed, lose heat and soon feel cool. This vasoconstriction suggests the possibility that the blood flow has been redistributed to preserve the supply to important structures at the expense of the skin. But such redistributions are also part of the mechanism for maintaining body temperature and may have no other significance.

Conclusions can only be based on consideration of all the relative factors. Conversely, the presumption that circulatory failure cannot occur in the absence of vasoconstriction is still less justified. Circulatory failure may develop in high output states without vasoconstriction. Adrenocortical failure, ganglion blocking and anti-adrenaline drugs, spinal block, deep anaesthesia and pyrexia may all be associated with circulatory failure in the absence of vasoconstriction. In all these states the blood flow through the tissues may not be significantly lowered in the early stages but eventually the skin will become cold. Slowing of the blood flow allows longer time for the extraction of oxygen and it should be remembered that just as cyanosis is only visible when the haemoglobin is in excess of a critical level, so also if constriction has emptied the capillaries of blood, cyanosis will not be obvious. However, in the lips, nose, ears and finger nails, peripheral cyanosis is usually easily detected. Generalized cyanosis of the skin is often seen during the induction of hypothermia especially when steps are not taken to counter the vasoconstriction. As the temperature falls a point is reached at which cyanosis disappears, due presumably to reduced oxygen extraction at the lower temperature.

The significance of peripheral cyanosis is merely the slowing of the peripheral circulation and its importance will depend on the cause—varying from cold to advanced circulatory failure. Peripheral cyanosis of the extremities can temporarily be improved by warmth and by rubbing, but the opening up of the skin vessels will only restore the skin colour if the arterial oxygen saturation is above about 85 per cent. If the saturation is below this level no improvement will result and the cyanosis must be regarded as central. Central cyanosis is seen not only in the cool areas, but also in the mucous membranes of the conjunctivae and inside the mouth; it may be due to inadequate ventilation, oxygen deprivation, pathological lung conditions or the presence of right-to-left shunts in the cardiovascular system. The two latter are often of long standing and may have led to clubbing and polycythaemia.

The state of filling of the veins is an important observation. When chronically over-filled, in the absence of venous obstruction, the most common cause is an increase in the blood volume. This is true also of the venous engorgement of chronic heart failure, although here there is also an element of back pressure. In recently developed states the venous engorgement is usually due to the back pressure of cardiac failure and may be exaggerated by over-transfusion. The possibility of pulmonary embolism or pericardial tamponade must be remembered when venous overfilling occurs with hypotension. While the state of filling of the neck veins is easily observed in a patient propped up and relaxed comfortably in bed, it is not so easy in the prone patient as the neck veins are, in any case, well filled. Sometimes sublingual veins, which are a few inches above the neck, can usefully be examined; even a limb can be raised and lowered, but obstruction at the thoracic inlet can be misleading, especially if there is any muscular effort by the patient. The height at which an intravenous infusion ceases to flow or, still better, the observation of a simple manometer connected to a three-way tap in the transfusion system may be employed. Particularly applicable to the recovery ward is a study of the veins on the dorsum of the foot. By stroking the veins to empty them and observing the time taken for refilling it is possible with practice to guess the venous pressure level. In the absence of cardiac failure in a warm patient, this information reflects changes in the blood volume and the need or otherwise for transfusion. A well-filled vein is sometimes viewed with undue alarm after cardiac surgery: it may be that a minor degree of venous distention may usefully increase the cardiac output in these circumstances. A raised central venous pressure is also often helpful during intermittent positive pressure ventilation to counter obstruction to cardiac filling by the raised intrathoracic pressure.

Under the conditions of anaesthetic work respiratory changes due to circulatory failure are difficult to detect until gross: at this stage, together with pupillary dilatation and the delta

rhythm on the e.e.g., they are signs requiring the most urgent correction to prevent irreversible cerebral damage.

Throughout this section the importance of adequate tissue perfusion with oxygenated blood has been emphasized; the expression blood pressure = cardiac output × total peripheral resistance being helpful in this connection. The equation is, however, only valid within reasonable limits: for example, it is not reasonable to expect much benefit from the use of extreme vasoconstriction when the cardiac output is markedly reduced except as a temporary expedient. The vasoconstriction may in itself—by depriving the tissues of blood—be the cause of anoxic damage and make recovery impossible. This latter concept has been invoked to support the use of vasodilator rather than vasoconstrictor agents in situations where "shock" might develop, the argument being that the perfusion, although at lower pressure, would reach the tissues through the dilated vessels. Low pressures will exaggerate the adverse haemodynamic effects of posture and also of any narrowing of blood vessels due to arteriosclerosis or other abnormality, and peripheral pooling will tend to lessen the venous return to the heart and this, together with the reduced coronary filling pressure, will not help the heart to increase its output to fill the dilated vascular bed. Sufficient expansion of this will inevitably result in a slowing of the capillary blood flow and an increased oxygen extraction. This may not be an adequate compensation and in extreme circumstances, just as in vasoconstriction, the result is tissue anoxia. While those familiar with vasodilator drugs and hypotensive techniques employ them with good effect, there is more general agreement about the benefits of vasoconstrictor drugs. Their use in circulatory failure in the absence of vasoconstriction can be most helpful. Even when vasoconstriction has occurred, but failure persists, they can assist mainly by a temporary increase of constriction thus breaking a vicious circle, and also in part by an associated inotropic or stimulant effect on the heart. Adrenaline and isoprenaline are really effective in this latter respect as is calcium chloride, particularly during massive transfusion. Members of the digitalis group are sometimes employed for this purpose. While this shows a very proper respect for tradition definitive benefit except in congestive heart failure and in tachycardia is rarely seen. Indirect measures such as improvement in oxygenation, the regulation of blood volume and the correction of acidosis are fundamental: without these, drugs can prove very ineffective.

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THE EVOLUTION OF ANAESTHESIA

BY

M. H. ARMSTRONG DAVISON

Department of Anaesthetics, Royal Victoria Infirmary, Newcastle upon Tyne, England

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OXYGEN

The first researches into the nature of air seem to have been made by J. B. van Helmont (1577–1644) who followed in the iatrochemical footsteps of Paracelsus and, like the latter, was imbued with *mystique*. It was van Helmont (1648) who invented the word "gas" (derived from the Greek word, *chaos*) and described a particular gas (gas sylvestre) which, in some respects is to be identified with carbon dioxide, but the difficulty of comprehending van Helmont's writings obscured the value of his discovery, and he influenced later workers but little.

John Mayow (1643–79), concerning whose life but little is known, came very near to the discovery of the true role of oxygen in respiration; today, his *Tractatus quinque medico-physici* (1674) is regarded as one of the greatest of the English medical classics, but the researchers who followed (Black, Priestley, and Lavoisier) were completely ignorant of his work. Mayow began with the premise that there was a "vital substance" present in air, and that this substance was essential for combustion. Since wet gunpowder will burn, Mayow postulated that this vital spirit was also present in nitre and he therefore named it the *spiritus nitro-aereus*. In confirmation of this theory, Mayow covered a lighted taper with a glass globe and showed that the flame went out when the nitro-aerial spirit was exhausted and, further, that the volume of air remaining had diminished in quantity. Mayow had already decided that the source of all heat was combustion or fermentation, the latter being a slow form of burning, and that in the living animal heat was produced in muscles. From this, he concluded that in respiration the "nitro-aerial spirit" was removed from the air in the lungs, absorbed by the blood, and carried to all parts of the body in the course of its circulation. He therefore repeated the experiment substituting a live mouse for the lighted taper, and achieved an identical result.

Mayow did not isolate oxygen, but he proved its existence, and his work ought to have been a beacon-light to those who were to come after him.

Eighty years passed before the chemical nature of air was further elucidated by Joseph Black, whose M.D. thesis of 1754 described the discovery of carbon dioxide, which he called "fixed air". In addition to the actual rediscovery of van Helmont's "gas sylvestre", Black (Singer, 1928), by means of his quantitative experiments with chalk, laid the basis for the atomic theory of John Dalton (1766–1844).

The actual isolation of oxygen was first achieved by Joseph Priestley (1733–1804) in 1771. Priestley, a Unitarian minister, had turned to teaching "natural science", as a means of eking out his small stipend when he held a ministry at Needham Market in Suffolk. The interest in science, thus aroused, remained with Priestley throughout various appointments; for instance, when he held a ministry at Warrington, he delivered a course of lectures on anatomy (Richardson, 1900). He also made numerous friendships in the scientific world, chief among which was a lasting bond with Benjamin Franklin. On removing to Mill Hill Chapel, Leeds, in 1767, Priestley interested himself in the chemical nature of air and, living next door to a brewery, carried out experiments with the "fixed air", which was available in abundance on the malting floor. Prevented because of his religious opinions from accepting the post of naturalist to Captain Cook's second voyage of discovery, Priestley remained at Mill Hill Chapel until, in 1773, he became librarian to Lord Shelburne (later Marquess of Lansdowne), a post in which he was able to

continue his scientific experiments without distraction.

In 1771 (as described in the Philosophical Transactions of the Royal Society), Priestley isolated a gas from nitre by heating it in a gun-barrel. He observed that a candle burned with an increased flame when immersed in this gas but, since he did not then possess a burning-glass, he was unable to produce the gas in sufficient quantities to examine its properties fully. It was not until August 1, 1774, that, having obtained a lens of 12 inches diameter and 20 inches focal length, Priestley obtained the same gas, which he called "dephlogisticated air" (oxygen) in considerable amount from *mercurius calcinatus*. A full description of the gas and the methods of obtaining it from mercuric oxide ("red precipitate") and red lead appeared in the *Experiments and Observations on Different Kinds of Air* (1774–75). In March 1775, Priestley showed that mice could live in this gas, and the discovery of oxygen with its potential use in medicine was put on record.

Priestley's chemical discoveries were numerous, but friction between him and Lord Shelburne led to the resignation of his post, and he returned to the ministry in Birmingham. He was a pronounced Liberal in his political opinions, and the support which he gave to a dinner to celebrate the anniversary of the French Revolution (July 14, 1791) led to an outbreak of mob violence in which his home was burned and the records of numerous experiments, never to be repeated or reported, were destroyed. In 1794 he emigrated to Virginia, where he continued his scientific work until just before his death in 1804 (Richardson, 1900).

Priority in the discovery of oxygen has often been claimed for the great Swedish chemist, Carl Wilhelm Scheele (1742–86). In fact, Scheele, by his own account, first isolated oxygen in 1772, and his first description of his discovery was not until 1777 (*Chemische Abhandlung von der Luft und Dem Feuer*), so there seems to be no doubt that both Priestley's discovery and his publication of it were first in the field.

The importance of oxygen in the economy of nature was further elucidated by Jan Ingen-Housz (1730–99). Ingen-Housz was a physician of Dutch origin; educated abroad and at Edinburgh, he settled in London; becoming in 1764, physician to the Emperor of Austria, he removed to Vienna. He contributed many papers to the Royal Society, and was elected a fellow on his return to England in 1778 (Harvey-Gibson, 1931). In 1779 he published his *Experiments on Vegetables*, in which he demonstrated the ability of green plants to absorb carbon dioxide when exposed to sunlight. This book is also important because at the end of the preface he wrote: "When this book was entirely printed, and nothing but the latter end of the preface unfinished, I was informed by my friend the Abbe Fontana [Felica Fontana, 1720–1805], that he discovered a few days ago a new method of procuring to a sick person the benefit of breathing any quantity of dephlogisticated air (oxygen) at a cheap rate." He goes on to describe the use of a solution of lime for the purpose of absorbing the "fixed air" (carbon dioxide), one of the earliest accounts of carbon dioxide absorption ever published. Scheele had also used "milk of lime" for absorbing "fixed-air" from the atmosphere of "fire-air" (oxygen) in which he kept bees alive.

It would seem from the above that the use of oxygen was already being advocated in medicine, but unfortunately we have no information concerning the circumstances in which it was recommended. The medicinal use of carbon dioxide was also advised at this time. Matthew Dobson (?1745–84), who is particularly remembered for his discovery that the urine of diabetic patients contains sugar, in his *Medical Commentary on Fixed Air* (1779), particularly recommends the use of carbon dioxide in putrid fevers; it was usually administered in the form of an effervescent drink, but sometimes as an enema.

By 1780, Chaussier of Dijon (Mushin and Rendell-Baker, 1953) was advocating the use of oxygen in the resuscitation of newborn babies, and he describes a mask and bag of chamois leather for this purpose. In the following year, Henry Cavendish (1731–1810) demonstrated that the combustion of hydrogen in oxygen produced water.

In the years 1780 to 1793 the understanding of the nature of chemistry was fundamentally changed by the work of Antoine Laurent Lavoisier (1743–94). This Frenchman, ably assisted by his young wife (she was fourteen years his junior), set up one of the finest laboratories

in the world at the French Arsenal. Among other great discoveries he showed the way in which acids and bases react to form salts, how oxygen and metals unite to form bases, and how oxygen and non-metals produce acids (Bernal, 1954). It was this last discovery which caused him to rename dephlogisticated air "oxygène", the acid-producer. The work of Lavoisier completely overthrew the phlogiston theory of Stahl and initiated a new era in chemistry.

In the field of biology, Lavoisier, assisted by Pierre de la Place (1749–1827) measured the metabolic rate and respiratory quotient of a pig (1780) and, with Seguin, of a man (1793). His experiments with living organisms demonstrated the true nature of respiration and its analogy with combustion and he achieved a quantitative analysis of these processes.

Lavoisier's last public service was to assist the commission which initiated the metric system of weights and measures. In 1793, he was arrested for his membership in the hated Ferme Générale, the tax-collecting authority of Royalist France, he was executed early in the following year. His widow subsequently became the wife of another great scientist, Count Rumford.

By 1788 both Edmund Goodwyn and Charles Kite were advocating oxygen in the treatment of asphyxia, and by the turn of the century the rationale of this treatment was universally accepted, but the difficulty of obtaining and storing supplies of gas prevented its use save in exceptional circumstances.

The foundation of the short-lived Pneumatic Institute at Clifton, near Bristol, increased the knowledge of gases, but the results in medical treatment were so unsatisfactory that the immediate effect was a withdrawal of interest from the subject. Thomas Beddoes (1760–1808), the founder of the Pneumatic Institute and the "discoverer" of Humphry Davy (1778–1829) was educated as a physician at Oxford, London and Edinburgh, in which latter University he obtained the degree of M.D. In 1787 he was appointed Lecturer in Chemistry at Oxford, a post which he was forced to resign after five years on account of his political opinions, which, like Priestley's, were Liberal; he also favoured the French Revolutionaries. While at Oxford, he published an account of the writings of John Mayow, and this work presumably drew his attention to the study of "airs" (gases) (Stock, 1811). The Pneumatic Institute was founded with the idea of studying the medicinal uses of various gases in which Beddoes had interested himself both before and after leaving Oxford, and Beddoes had definite views on the function of oxygen in the animal economy. He followed Lavoisier, in opposition to many other scientists of his time, in believing that oxygen was removed from the air in the lungs and carried in the blood to different parts of the body, where it acted by increasing the "irritability" of living tissues; he also believed that sleep was caused by a reduction of oxygen in the body; and he considered pulmonary tuberculosis to be caused by an excess of oxygen; he therefore recommended treating that disease by inhalations of carbon dioxide. Scurvy, on the other hand, he thought was due to the removal of oxygen from the air by the action of intense sunlight. On the whole, he regarded pure oxygen as poisonous, although the presence of some oxygen in the atmosphere was essential to life; and Humphry Davy held similar views (Cartwright, 1952).

The fact that, unlike lighted tapers and living animals, green plants were not killed by enclosing them beneath a glass globe, puzzled John Mayow. As we have seen, Ingen-Housz had gone some way to explain the paradox, but the full explanation came from Theodore de Saussure (1767–1845) of Geneva, who demonstrated the essentials of plant nutrition in 1804 (Singer, 1950). He also showed that the seeds of plants will not germinate in the absence of oxygen, that carbon dioxide retards germination, and that light has no effect on germination until after green leaves have appeared.

In 1809, William Allen and W. H. Pepys read a paper entitled "On respiration" at the Royal Society, detailing careful quantitative experiments in which they showed that the only change which occurs to air during respiration is the substitution of carbon dioxide for a portion of the oxygen and that, when pure oxygen is breathed, nitrogen is excreted through the lungs. They also showed that the earliest scientists were wrong in believing that the lungs were completely collapsed after expiration and, in fact, still retained more than 100 cubic inches of air.

By the early nineteenth century, the value of oxygen in certain cardiac conditions was beginning to be recognized. In 1817, a Dr. R. Read delivered a paper in Dublin, "On the use of oxygen gas in angina pectoris" (Foy, 1889); he described a typical case of angina in a man of 66 who was much relieved by the inhalation of several quarts of the gas. However, as was natural in the unsatisfactory state of medicine at that time, oxygen came to be used as a sort of panacea, and failing in that purpose, was largely discarded. Thus we have an account (Anonymous, 1856) of one Daniel Hill, a practitioner in Bloomsbury in the early years of the nineteenth century: starting with the perfectly reasonable idea that "in all cases of debility, where the action of the heart and arteries was weak, it [oxygen] should prove extremely beneficial to the patient." He had some success in such cases, but Dr. Hill proceeded to use the gas in the treatment of all sorts of complaints, and claimed success with it in the treatment of epilepsy, paralysis, arthritis of the knee, tuberculosis of the hip, and other conditions. An account of one such patient is too remarkable to be omitted here.

> Hydrocephalus—child of William Bennet, seventeen months old. At six months had small pox, succeeded by epilepsy; then inflammation of the eyes; after which the head began to enlarge until the sutures opened to a considerable extent and allowed the fluctuation of the water to be distinctly felt through the membranes. Pulse weak, beating 100 per minute, pressure on brain had caused total paralysis of extremities. Case was considered hopeless, oxygen treatment tried; in one week the child began to show improvement; in a month the head was reduced nearly to its natural size, the paralysis of the limbs was cured, and by continuing the treatment perfect recovery was soon accomplished.

We are not surprised to read that "Mr. Hill's treatment appears to have met with much hostility from his medical brotherhood"; honest physicians would not believe such reports, and hostility to such practitioners naturally entailed a decreased interest in the already proved virtues of oxygen.

However, the general public was becoming better informed of the truths of chemistry, and this interest was bound, sooner or later, to be reflected in medical practice. The biggest forward step was taken when, in 1844, Horace Wells made his ill-fated attempt to introduce anaesthesia with nitrous oxide. In 1845, George Wilson, M.D., F.R.S.E., Lecturer in Chemistry at Edinburgh, read a paper before the Royal Scottish Society of Arts, "On the employment of oxygen as a means of resuscitation in asphyxia." In this paper, he first argues the value of early and effectual artificial respiration and then goes on to claim—on physiological grounds—the superiority of oxygen over common air for this purpose. He then proceeded to describe simple apparatus from which, by heating potassium chlorate mixed with ferric oxide, an adequate and cheap supply of oxygen could easily be obtained. Recognizing the difficulty of introducing the gas into the lungs of the patient, Wilson devised a species of oxygen "tent" which might be made of

> . . . wickerwork covered with waterproof cloth. It should be large enough to contain the head and neck of the patient, and the front should be hinged so that it might be thrown open at once if necessary and glazed so as to permit the patient's face to be seen. The side of the box where the patient's head was introduced, might be terminated in a cylinder or loose tube of waterproof cloth, which could be tied round the neck by a ribbon or be attached to the skin by a piece of sticking plaster, so as to prevent escape of oxygen.

Allowance for the evacuation of the respired air was made and artificial respiration, by compression of the chest, was not impeded by the apparatus. Wilson thought that all the above materials should be available at "our public hospitals, lying-in institutions, humane societies' rooms, police office stations and wherever else cases of asphyxia frequently come." He continued:

> The method appears particularly applicable to midwifery hospital practice. The quantity required for the inflation of the lungs of a still-born [*sic*] infant could easily be supplied by even a small apparatus. The method proposed would apply to every form of asphyxia occurring in hospital practice, to cases of poisoning with opium and to other states of disease or injury.

In spite of ingenious suggestions of this sort the use of oxygen in medical practice, other than very occasionally, was limited by the size of gasholders and the inability to transport gas other than for short distances and in only small quantities in bladders. It is not known when oxygen was first compressed into metal cylinders, although it is known that the Viennese fire brigade employed cylinders of compressed air as early as 1833 (Cooper, 1960). In London, cylinders of compressed oxygen were available at least as early as 1856 (Anonymous, 1856), but it was not for another fifteen years that they were in much demand.

John Snow (1858) recorded one instance of death under chloroform anaesthesia in 1849 in which oxygen was used in an unsuccessful attempt at resuscitation, but this must have been extremely rare at that date, for oxygen was apparently usually prepared on the spot. The intensive use of cylinders began with the work of the firm of Barth in 1868, quickly followed by that of Coxeter.

Cylinders were apparently not in use in America at this time, for when E. Andrews, Professor of Surgery at the Chicago Medical College, introduced the idea of mixing nitrous oxide and oxygen in order to obtain improved "gas" anaesthesia in dentistry, he complained of the cumbersome bulk of balloons for storage and transport (Duncum, 1947).

The revolutionary idea of combining oxygen with nitrous oxide did not at first meet with great success, and in 1872 we find Alfred Coleman writing "that mixtures of nitrous oxide and oxygen in various proportions had been employed, but that they had not been attended with success; they produced much struggling and excitement with but imperfect anaesthesia" (Duncum, 1947).

However, in 1878, Paul Bert (1833–86), Professor of Physiology at the Sorbonne, began to experiment with prolonged nitrous oxide anaesthesia, achieved by administering the gas mixed with air at a raised pressure. A year later, he was using 85 per cent nitrous oxide with 15 per cent oxygen at a pressure of 920 mm Hg with great success. Unfortunately the restrictions of the pressure chamber which had to be used as an operating theatre were such that by 1883 the method was virtually abandoned, even by Bert, who, however, thought that "this method of anaesthesia as nearly as possible approached perfection" (Duncum, 1947).

The interest which had been aroused in prolonged anaesthesia by Bert's method led to several attempts to use a mixture of nitrous oxide and oxygen at normal pressure. The first to be successful was said, by Hewitt (1901), to have been Klikowitch of St. Petersburg, probably in 1881. Hewitt himself experimented with the mixture, using for the purpose a calibrated gasometer which could be filled with the gases in any desired proportion. The first successful portable apparatus appeared in 1886; it was that of H. T. Hillischer, a Viennese dentist (Duncum, 1947).

Hewitt found Hillischer's apparatus unsatisfactory because the regulating valve could not be adjusted "with that nicety which is necessary in actual practice": he therefore set about designing an improved machine. This was first described in 1893 and it was followed in 1897 by a still more satisfactory apparatus (Duncum, 1947). As a result of all these endeavours, the idea of nitrous oxide-oxygen anaesthesia became widespread. Almost contemporaneously the idea of giving oxygen with other volatile anaesthetic agents was introduced. In 1887, Neudörfer of Vienna proposed the routine administration of oxygen with chloroform, and this suggestion was acted on by Kreutzmann of San Francisco, who employed Junker's vaporizer for this purpose. In 1895 a large series was reported by H. L. Northrop, and at the same time T. S. K. Morton of Philadelphia began using oxygen with ether, adopting an oxygen inhaler made by the S. S. White Dental Manufacturing Co. for this purpose (Thatcher, 1953). Meanwhile, in Europe, L. Prochownick of Hamburg began to use oxygen routinely at the end of anaesthesia with the idea of improving the patient's general condition in the immediate postoperative period. An important part of Prochownick's apparatus was the reducing valve. This apparatus was modified by Wohlgemuth in 1901; in 1902, Roth of Lübeck introduced a "bubble vaporizer," and added a reservoir bag to Wohlgemuth's oxygen - chloroform apparatus (Duncum, 1947). The subsequent development of anaesthetic machines has been dealt with already in the section on nitrous oxide.

As early as 1588, de Acosta had reported that air above 14,000 feet was not suitable for respiration. The introduction of the hot-air balloon by the brothers Montgolfier in 1782 was to open a new era in the history of man's endeavour. The first human being to ascend in a balloon was de Rozier of Metz in 1783, but great heights were not easily obtained; in 1804, Gay-Lussac and Biot ascended to 13,000 feet, but it was not for another half-century that greater heights were reached. In 1862, Glaisher and Coxwell reached 29,000 feet and suffered severely from oxygen want. Advised by Paul Bert, Croce-Spinelli, Sivel and Tissandier carried oxygen with them in their ascent of 1875, but it did not prevent the two former from dying of anoxia, since they became unconscious too suddenly to be able to avail themselves of the gas.

Tissandier was more fortunate, and the oxygen undoubtedly contributed to his survival. In all later high ascents oxygen was, of course, carried. With the advent of the aeroplane and the considerable heights achieved during the first Word War, much ingenuity was used in designing suitable oxygen apparatus for aviators. Mountaineers benefited from this work, and oxygen apparatus was carried in the attempts to scale Mount Everest in 1922 and on subsequent occasions. It is not without interest that the Everseal masks (Medical & Industrial Equipment Co. Ltd.), commonly used in this country in anaesthetic practice, were designed for use by Sir John Hunt's team which conquered Mount Everest in 1953.

Textbooks of anaesthesia in the nineteenth century have but few references to oxygen. A book published in 1879 (Turnbull), for instance merely mentions oxygen in order to deny that it is an anaesthetic. The first edition of Hewitt's textbook (1893) does mention the use of oxygen in respiratory emergencies, but only very briefly and not much in its favour; the paragraph is unchanged in the second edition (1901). However, Dudley Buxton was, by 1900, advocating oxygen in the treatment of laryngeal spasm and of chloroform "syncope". Indeed, it was not until after the end of the first World War that the use of oxygen in resuscitation became at all normal. A certain "Captain Stokes" is credited by Barach (1944) as having introduced the use of oxygen by nasal catheter in the treatment of pulmonary oedema caused by gas poisoning, but this easy and efficient method of administration was soon forgotten and oxygen chambers were devised by Barcroft in England and by Stadie of the Rockefeller Institute, largely as the result of the influential paper by Haldane (1917).

The first oxygen tent to fit over the bed was described by Leonard Hill in 1920 (Barach, 1944), but the apparatus was not satisfactory since there was no means of removing excess moisture and heat. This difficulty was overcome by A. L. Barach who constructed an oxygen tent in which oxygen-enriched air was blown over ice, thus cooling and drying the atmosphere.

Efficient masks for the administration of oxygen were introduced in 1938 (Bulbulian) when the "B.L.B." (Boothby, Lovelace and Bulbulian) apparatus was described, and there have been modifications and improvements in such devices at frequent intervals ever since.

As the value of oxygen has become more apparent the price has been reduced, and the means of supply have been improved. Many hospitals now have a piped oxygen supply not only to the operating theatres, but also to the wards. It is a far cry to the days when Charles Kite (1788) wrote of the costliness of procuring sufficient oxygen ("about two hogsheads") for a single case of respiratory failure.

HELIUM

The discovery of helium, identified in the sun twenty-seven years before it was isolated on earth, is one of the most remarkable passages in the history of science. It was in 1868 that Sir Norman Lockyer investigated the rays of the sun with a spectroscope: he noticed a fine yellow line close to the sodium pair, and, since no other substance known to science gave this line, he concluded that he had found a new element, which he named helium, from the Greek word for the sun. In 1895, Sir William Ramsay, examining a rare Norwegian mineral called "cleveite", obtained from it a gas which gave an identical spectrogram (Harvey-Gibson, 1931).

Helium, one of the "inert" gases, is non-inflammable. At the outbreak of the first World War, observation balloons were filled with hydrogen and were consequently extremely dangerous and easily destroyed by enemy action. Helium occurs naturally in large quantities only in the natural gas fields of North America, whence it was imported into England in large quantities to replace hydrogen for balloons.

Mixtures of helium and oxygen were first used for inhalation by the American chemist and physicist, Elihu Thompson, who found that it was ideal for use by deep divers. A mixture of helium 80 per cent and oxygen 20 per cent has a density roughly one-third that of air or pure oxygen, hence in conditions of turbulent flow, when the density of the gas is important, the helium mixture can be made to flow with much less effort than either air or pure oxygen. On these grounds Barach, in 1934, recommended the use of this mixture for the treatment of asthma and allied conditions. Since masks at that date were not satisfactory, and the high difusibility of

helium renders a tight-fitting mask essential, Barach and Eckman designed a helmet, fitting closely round the neck, for use with helium mixtures. The enthusiasm with which this gas was first hailed has waned considerably; it is now recognized that, even in asthma, laminar flow, in which the viscosity of the gas is more important than its density, is present in a large component of the respiratory passages. Since the viscosity of helium is very high, its advantages in inhalational therapy are negligible.

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BOOK REVIEW

Die kuenstliche Hibernation. By Prof. Dr. med. P. Véghelyi. Second (first German) edition. German translation by A. Faragó. Published by Akadémiai Kiadó, Budapest, 1960. Pp. 612. Price £6 10*s.* 0*d.*

This interesting monograph deals with artificial hibernation, with and without hypothermia, as it is practised at university institutes in Hungary. It is a comprehensive work which starts by posing the problem of seemingly irreversible shock and the possibility of overcoming it by reducing oxygen demand. It proceeds to discuss the physiology of hibernation in animals and in man, the physiology and techniques of hypothermia, goes on to consider the pharmacology of drugs used for hibernation [with the accent on chlorpromazine] and then reports on the development of the method, its reception in various countries and on the latest theories which explain its successes. After listing the various "disconnecting" mixtures now in use, the author describes his method, equipment, and techniques for medical and surgical hibernation. His own results are reported as well as those of many others, in all branches of surgery, in allergy, shock, perinatal, respiratory and circulatory disturbances, in psychiatry and in cases of poisoning. The volume ends with a chapter on contra-indications and undesirable side effects.

It is a tremendously industrious work. The author seems to have collected all the available literature in English, French, German, Italian, Spanish, Russian and, of course, Hungarian up to June, 1959, comprising 1,568 references. A great deal of his own and his collaborators' research and their clinical experience in 5,600 cases has been incorporated, with well-drawn figures and clinical record cards, respectively. In the theoretical as well as in the clinical part opinions and results differing from the author's are described and discussed, so that an all-round picture is presented of this method of treatment which has been widely used and for which even further fields of application are suggested.

A theoretical "Leitmotiv" runs throughout the work: In shock, haemorrhage or stress the body reacts with peripheral vasoconstriction which is at first effective as it ensures the blood supply of the vital organs. Eventually this endeavour of the organism will result in exhaustion by leading to oxygen requirements which cannot be met and the body succumbs to tissue hypoxia. High fever, sepsis, severe peritonitis, toxaemia of infants and many other conditions may also end fatally due to unfulfilled oxygen demand. The accepted treatment has been to sustain this vasoconstrictor reaction with vasopressors and analeptics until the underlying causes, such as blood loss, bacteraemia or dehydration, have been remedied. But the logical procedure is to reduce the oxygen demand of the tissues by sedatives, analgesics, vegetative blocking agents and cooling of the body while specific treatment is given.

Cooling can often be sufficiently achieved by the use of "disconnecting" drugs alone and the resulting balance between oxygen demand and supply expresses itself in reduced pulse and respiratory rates, and in the disappearance of cyanosis and restlessness. In severe cases, and in special operations as may occur in cardiac surgery, hypothermia has to be added; this is produced by surface cooling. In shock, cooling has to be undertaken together with hibernation as the vasoconstriction caused by the latter will further reduce the circulating blood volume. One interesting point is the author's favourable experimental and clinical experience in cases of renal ischaemia and shock oliguria or anuria.

The drugs used vary with the indications. The "Classical cocktail", consisting of promethazine, chlorpromazine and pethidine in the ratio of 1:1:2, is used for medical cases. If parasympathetic depression is desired diethazine is added in a dose 5 times that of chlorpromazine. In surgery the latter is usually replaced by Hydergine 0.3 to 0.6 mg; this avoids tachycardia, paralyzes the thermoregulation for longer periods and is without undesirable effects on heart muscle and brain.

The doses used will appear very large to British anaesthetists. The preparation for combined hypothermia and hibernation for a 45-kg patient starts 2½ hours before induction with the administration of Hydergine 0.3 mg, promethazine 50 mg, pethidine 100 mg, and Vit. B_1 200 mg. This is followed one hour later by Hydergine 0.6 mg, promethazine 50 mg and pethidine 100 mg, and half an hour before induction by chlorpromazine 25 mg and pethidine 100 mg; in all 300 mg of pethidine is given pre-operatively in a slight patient. Induction is carried out as usual with a small dose of ultrarapid-acting barbiturate, followed by suxamethonium, oxygenation and intubation. Further relaxation is obtained by d-tubocurarine, and anaesthesia is deepened to the second plane using ether—which is said to maintain the sinus rhythm at very low temperatures—or halothane. But in cardiac surgery, two minutes before the large vessels are clamped suxamethonium is given again, after d-tubocurarine. No cardiac irregularities are expected at temperatures down to 26°C if the thorax remains closed. Rewarming of deeply cooled cases is to be slow and, if not needed earlier, a dose of the "cocktail" is given when a temperature of 36.5°C has been reached. Drug hibernation has to be continued over 1 to 2 days and has to be reduced slowly. In medical cases it has been continued over long periods.

The author reports on 450 medical cases in whom treatment was started when the patients were in extremis. Of these 162 died, and 217 could be followed up; 164 of these had recovered completely, the rest partially.

The book should not prove difficult to read for those familiar with scientific German, though the style is not as concise as in English medical literature. The meaning is always clear, the print good, the index satisfactory and the list of references excellent. A novel feature is a pocket fixed to the inside of the back cover which contains exact rules printed on cardboard, for various techniques of hibernation. Such an arrangement might be useful for textbooks

on anaesthesia, dealing with such emergencies as cardiac arrest, vomiting, laryngospasm.

It would be well worth while to arrange for an English edition of this thorough treatise on an entirely different approach to the problems of shock, stress and unsatisfied oxygen demand.

Luise Wislicki

Essays on the First Hundred Years of Anaesthesia, Vol. 2. By W. Stanley Sykes. Published by E. and S. Livingstone Ltd., Teviot Place, Edinburgh. Price 30*s*.

Having read this second volume of essays the uppermost feeling in one's mind is the impression of the immense amount of care that Dr. Sykes took to collect the information that he gives us. Next to that is the charming way in which he deals with it. Here he is at pains to stress the value of history and by way of illustration he begins with a chapter on thirty-seven different ways in which patients have lost their lives. A careful perusal of this chapter should go far to prevent a repetition of them. Improvements in apparatus have already eliminated some. The decline in the number of deaths due to anaesthetics from 916 in 1938 to 751 in 1946 "appears to be a notable achievement", considering the increasing severity and duration of operations, and is mostly due, Dr. Sykes thinks, to the "widespread availability of trained anaesthetists".

The chapter on the "Renaissance of $CHCl_3$" underlined by "Progress forward or backward?" leaves no doubt in the mind of the reader that the author thought it backward. After wading through some thousands of pages of British and American textbooks in search of information about anaesthesia in heart cases, what he found "was for the most part vague, sketchy, and of little practical use. Moreover most of it was obsolete".

However, this search was not fruitless. It gave rise to the idea of training a young anaesthetist in cardiology and encouraging him to apply his knowledge to the investigation of the effect of anaesthesia on the human heart. Dr. Sykes adds that having been out of touch with the practice of anaesthesia for fifteen years it is possible that the idea has been anticipated. He was right: it has. Anyone acquainted with modern anaesthesia reading Dr. Syke's requirements would immediately think of Michael Johnstone as fitting the picture. He is young in years, old and experienced in cardiology and anaesthesia, and especially so in the application of cardiology to anaesthesia. It is twelve years since he published his first paper on "General anaesthesia and cardiac inhibition", in which, among other things, he advocated the increasing use of the electrocardiograph, and practised his preaching, as we see in the numerous papers he has published since that time. With the new techniques constantly appearing, as, for example, the hypotensive and the hypothermic, it is of the highest importance that their effect on the heart should be accurately appraised. For this purpose we need anaesthetists capable not only of taking an electrocardiogram but of accurately interpreting the significance of its hieroglyphics, a much more difficult task. Dr Sykes begins this chapter with a picture of Mackenzie, whom he calls the founder of modern cardiology, and concludes it with a drawing of his ink polygraph.

The next picture is of Marcel Garcia, the founder of laryngoscopy, a famous teacher of singing who lived for 102 years and was present at the centenary banquet given in his honour. The chapter dealing with this is mostly about the various methods of intubating the larynx. It gives a special commendation to the Kuhn's tube in that it is not dependent on batteries nor does it age as those of indiarubber do. In the days immediately preceding the 1914 war and while it continued the Kuhn's tube was one of the best ways of giving $CHCl_3$, it provided an open airway and the attached auscultation tube enabled one to hear every breath. A little conscience-stricken perhaps, Dr. Sykes having said what he describes as "some very hard things" about Charles T. Jackson, in his first edition, devotes a whole chapter to Jackson's defence of himself. Three short classical articles follow dealing with the discovery of $CHCl_3$ by Simpson, Horace Wells's letters from prison, and Mr. James Moore's account of his compressor.

The fallibility of clever men when they forsake their own jobs and attempt to prophesy is the subject of a short but amusing chapter.

The book concludes with an account of the death of Miss Wyndham, nitrous oxide's first victim, the early use of rectal ether, $CHCl_3$ before Simpson, and intravenous injection of hedonal which I saw Moynihan's anaesthetist using at Leeds.

Unfortunately, owing to Dr. Sykes's death, we cannot expect any more essays on the first 100 years from his pen, but the subject is by no means exhausted. Spinal anaesthesia, about which opinions differ so much, played a considerable part in the history of the first 100 years of anaesthesia and yet it is scarcely mentioned. If Wayne Babcock was right when he said: "In no other known way can so profound and extensive an anaesthesia be produced by so small a dose of a drug and with so little toxicity" and "After a death under spinal anaesthesia the anaesthetist may often write his own name in the space of the certificate reserved for the cause of death", it would seem, as Cassius once said, "The fault, dear Brutus, is not in our stars but in ourselves", and if so this excellent method applied by better trained anaesthetists will take its rightful place in the next 100 years.

Another subject which calls for appropriate treatment in any history of the first 100 years is that of the changed position of the anaesthetist. Apart from the statement that he could not make a living out of anaesthesia before the war of 1939–45 he does not refer to the matter. If any of the older generation of anaesthetists are still living and can find time to jot down their reminiscences such records might prove valuable to any future writer of historical essays.

Dr. Sykes has written a book of absorbing interest, particularly perhaps to those of us who have lived through a considerable section of the period. It is profusely illustrated, well printed and indexed, and cheap only in its price.

E. Falkner Hill

UNIVERSITY OF CAMBRIDGE POSTGRADUATE MEDICAL SCHOOL

SYMPOSIUM ON PAIN

to be held at Addenbrooke's Hospital, Cambridge, on

SATURDAY, DECEMBER 9, 1961

Morning session

10.30 THE NEUROPHYSIOLOGY OF PAIN
G. S. Brindley, M.D., Department of Physiology, University of Cambridge

11.30 COFFEE

11.45 (*a*) THE RESPONSE OF ANIMALS TO DRUGS IN THE NORMAL AND THE ANAESTHETIZED STATES

(*b*) MANAGEMENT OF CANCER PAIN WITH OPIATES AND TETRAHYDROAMINACRINE

Professor F. H. Shaw, Department of Pharmacology, University of Melbourne

Afternoon session

2.30 THE ANALGESIC SUPPLEMENTATION OF GENERAL ANAESTHESIA
Professor T. C. Gray, Department of Anaesthesia, University of Liverpool

3.30 PHENOL NERVE BLOCK IN THE TREATMENT OF INTRACTABLE PAIN
H. R. Youngman, M.D., F.F.A.R.C.S.,
Department of Anaesthetics, United Cambridge Hospitals

4.30 TEA

These meetings are open to anaesthetists of all grades and any members of other Departments who are interested. Course fee £1 1*s.*; charge for buffet lunch at the hospital 4*s.* 6*d.*

Those intending to attend are asked to notify the Secretary of the Medical School, Tennis Court Road, Cambridge, *before December* 2, 1961, if possible, stating whether lunch is required and enclosing the appropriate fee.

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Programme for Session 1961–62

1961

FRIDAY, OCTOBER 13, 8 P.M.

Ordinary General Meeting at the Liverpool Medical Institution.

Speaker : Professor GRAY.
Some Highlights and Impressions of my Tour.

FRIDAY, NOVEMBER 24, 8 P.M.

Ordinary General Meeting at the Liverpool Medical Institution.

Speaker : Dr. W. D. WYLIE.
Anaesthesia in the Labour Ward.

1962

THURSDAY, JANUARY 11, 8 P.M.

Joint Meeting with the Liverpool Medical Institution at the Liverpool Medical Institution.

Symposium : Open Heart Surgery in Children with Extra-Corporeal Pump.

Speakers : Mr. F. RONALD EDWARDS.
Dr. R. S. JONES.
Dr. G. JACKSON REES.
Dr. A. L. STEAD.

1962

FRIDAY, FEBRUARY 23, 8 P.M.

Ordinary General Meeting at the Liverpool Medical Institution.

Speaker : Professor W. D. M. PATON.
Theories of Action of Neuromuscular Blocking Agents.

FRIDAY, MARCH 16, 8 P.M.

Ordinary General Meeting at the Liverpool Medical Institution.
Papers to be Presented by Registrars.

THURSDAY, APRIL 12, 8 P.M.

Combined Meeting with the Anaesthetic Section of the Manchester Medical Society, in Manchester.

Speakers :
To be announced later.

FRIDAY, MAY 11, 8 P.M.

Thirtieth Annual General Meeting at the Liverpool Medical Institution.

FACULTY OF ANAESTHETISTS
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Course on Anaesthetics for Consultants and S.H.M.O.s

A three-day course on Anaesthetics for Consultants and S.H.M.O.s will be held from November 2 to 4, 1961. There will be twelve lectures on topics of general interest, each followed by a discussion period. The fee for the course is five guineas, including coffee, lunch and tea in the College.

Applications should be sent as soon as possible to Mr. R. S. Johnson-Gilbert, M.A., Secretary, Faculty of Anaesthetists, Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2 (Tel. HOLborn 3474, extension 23).

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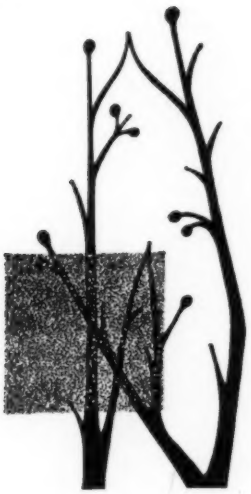

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